

Corbus Pharmaceuticals, Inc.

Protocol Number: JBT101-DM-002

**A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3
Trial to Evaluate Efficacy and Safety of Lenabasum in Dermatomyositis**

May 26, 2021

Statistical Analysis Plan

Version 1.0

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1 LIST OF ABBREVIATIONS AND GLOSSARY OF TERMS

1.1 List of Abbreviations

5-D Itch	Five-dimension itch questionnaire
AE	Adverse event
ACR	American College of Rheumatology
ALT	Alanine aminotransferase
ADM	Amyopathic dermatomyositis
AST	Asparagine aminotransferase
ATC	Anatomical Therapeutic Chemical
BID	Twice per day
BMI	Body mass index
CDASI	Cutaneous Dermatomyositis Disease Area and Severity Index
CI	Confidence interval
CK	Creatine kinase
COVID-19	Coronavirus Disease 2019
CT	Computerized tomography
DM	Dermatomyositis
DMC	Data Monitoring Committee
DOI	Definition of Improvement
ECG	Electrocardiogram
EMGA	Extramuscular Global Assessment
EQ-5D-5L	European Quality of Life Five Domain, Five Level Questionnaire
EULAR	European League against Rheumatism
FACIT-F	Functional Assessment of Chronic Illness Therapy – Fatigue Questionnaire
FDA	Food and Drug Administration
FVC	Forced vital capacity
HAQ-DI	Health Assessment Questionnaire – Disability Index
IGA	Investigator Global Assessment
ILD	Interstitial lung disease
IST	Immunosuppressive therapies
IV	Intravenous
IWRS	Interactive web-based randomization system
LDH	Lactic dehydrogenase
LOCF	Last observation carried forward
LS	Least squares
MedDRA	Medical Dictionary for Regulatory Activities

Max	Maximum
MDGA	Physician Global Assessment
MID	Minimal important difference
Min	Minimum
mITT	Modified intent-to-treat
MMRM	Mixed effect model for repeated measures
MMT	Manual Muscle Test
MMT-8	Manual Muscle Test that assesses 8 muscle groups
PK	Pharmacokinetic
PP	Per protocol
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29 item (questionnaire)
PtGA	Patient Global Assessment
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
SF-36	Short Form 36-question health survey
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TIS	Total Improvement Score
VAS	Visual analog scale

1.2 Glossary of Terms

Adverse event:	<p>Any untoward medical occurrence in a patient or a clinical investigation subject administered a medicinal product which does not necessarily have a causal relationship with this treatment.</p> <p>An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a study product, whether or not related to the study product. Intercurrent illnesses, injuries or any event of abuse, misuse or addiction are also considered adverse events. For marketed medicinal products, this also includes failure to produce expected benefits (i.e., lack of efficacy), abuse, or misuse.</p>
Blinding:	<p>A procedure in which 1 or more parties to the trial are kept unaware of the treatment assignment with the intent to reduce the risk of biased outcomes.</p>
Completed:	<p>Subject who completed the last protocol-defined visit.</p>
Eligible:	<p>Qualified for enrollment into the study based upon strict adherence to inclusion/exclusion criteria.</p>
Study product:	<p>A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial.</p>
Life-threatening:	<p>The term “life-threatening” in the definition of “serious” refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.</p>
Protocol amendment:	<p>As defined by the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice: “A written description of a change(s) to or formal clarification of a protocol.”</p>
Serious adverse event:	<p>An untoward medical occurrence that at any dose (a) results in death, (b) is life-threatening, (c) requires inpatient hospitalization or prolongation of existing hospitalization, (d) results in persistent or significant disability/incapacity, (e) is a congenital anomaly/birth defect, or (f) results in an important medical</p>

event that may jeopardize the patient and may require intervention to prevent one of the other outcomes.

Subject:	Term used throughout the protocol to denote an individual that has been contacted to participate in the clinical study, either as a recipient of the study product or as a control.
Subject Identification Number:	A unique number identifying a treatment to a subject, per the study randomization.
Suspected Unexpected Serious Adverse Reaction:	An adverse event that (a) meets the definition of a serious adverse event, (b) the nature or severity of which is not consistent with study product information in the Investigator's Brochure, and (c) there is reason to suspect that the study product caused the event.
Tolerability:	The incidence of discontinuation of study product or study discontinuation due to a treatment-emergent adverse event probably or definitely related to study product.
Treatment:	Term used throughout the protocol to denote the study product or placebo intended to be administered to a subject.
Treatment-emergent adverse event:	Any event not present before the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments.
Twice per day dosing:	Two doses each day with at least 8 hours between doses and without requirements for fasted or fed state.

2 INTRODUCTION

This statistical analysis plan (SAP) is being developed in conjunction with the protocol JBT101-DM-002 (Version 2.2, and Version 2.3 [Japan] dated 13 January 2021) sponsored by Corbus Pharmaceuticals, Inc. The SAP contains detailed information to aid in the performance of the statistical analysis and reporting of the Part A data for use in the final Clinical Study Report (CSR). A separate SAP for study JBT101-DM-002 will be prepared for the Part B open-label extension data.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonisation E9 Guideline entitled: Statistical Principles for Clinical Trials and the most recent International Conference on Harmonisation E3 Guideline entitled: Structure and Content of Clinical Study Reports.

This SAP describes the data that will be analyzed and the subject characteristics, efficacy, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used.

The SAP will be finalized before database lock and unblinding. If the Food and Drug Administration (FDA) requests additional analyses after the SAP is signed, those analyses will be done and added as an amendment to the SAP as additional analyses requested by the FDA. Otherwise, there will be no changes by the Sponsor to this SAP after database lock. If any additional analyses other than those requested by the FDA are required to supplement the planned analyses described in this SAP, those ad hoc analyses will be identified as such in the CSR.

3 OBJECTIVES

3.1 Primary Objective

To evaluate the efficacy of lenabasum compared to placebo in subjects with dermatomyositis (DM).

3.2 Secondary Objective

To evaluate the safety and tolerability of lenabasum in subjects with DM.

3.3 Tertiary Objectives

- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

4 INVESTIGATIONAL PLAN

4.1 Study Design and Plan Description

This is a Phase 3, multicenter, interventional, double-blind, randomized, placebo-controlled study designed to assess the efficacy and safety of lenabasum in subjects with DM.

The study consists of 2 parts:

- Part A: Double-blind, placebo-controlled phase
- Part B: Open-label extension phase (optional)

The overall design for this study is summarized in Figure 1 of the protocol.

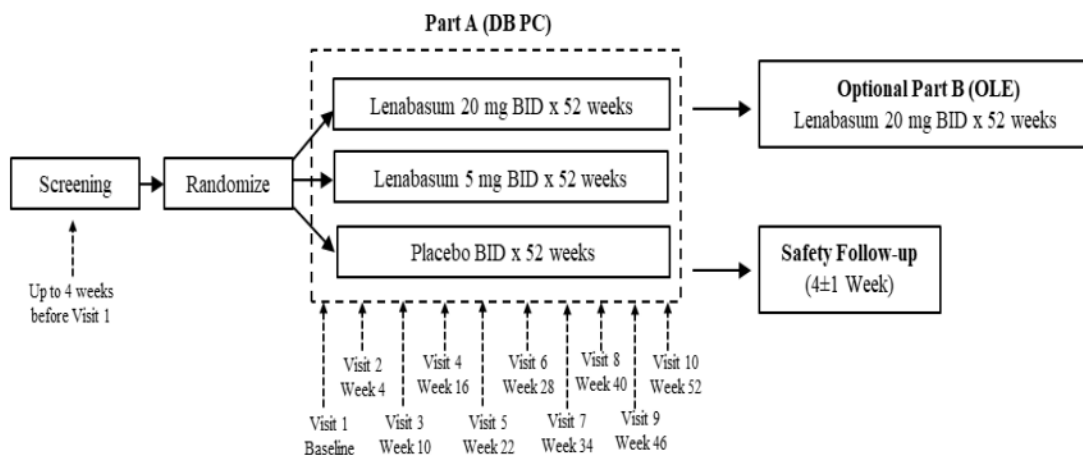
Part A Double-Blind, Placebo-Controlled Phase

The initial plan is for approximately 150 dosed subjects to receive at least 1 dose of study product. The final number of subjects to be dosed will be determined after a blinded interim analysis of variability of the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Myositis Response Criteria Total Improvement Score (TIS) (Lundberg et al, 2017). The blinded interim analysis will be performed when approximately 30 subjects have at least 6 months of efficacy data.

Subjects will be randomized to receive lenabasum 20 mg, lenabasum 5 mg, or placebo, all twice per day (BID), in a 2:1:2 ratio.

The total duration of participation for an individual subject is approximately up to 60 weeks and includes the following: a screening visit (up to 4 weeks before Visit 1), up to a 52-week treatment period, and a Safety Follow-up Visit that will be conducted 4 ± 1 weeks after the last visit. Subjects can opt to participate in an open-label extension after completing the double-blind Part A of the study. Subjects will be assessed for safety and efficacy parameters every 6 weeks (except for Visit 2, which will occur 4 weeks after Visit 1) for a total of up to 10 treatment visits. Study personnel will also contact subjects by telephone halfway between Visit 9 and Visit 10 (Week 49 ± 2) to assess compliance, safety and overall status of DM, if applicable.

Figure 1. Part A Schematic



The schedule of Visits and Assessments is presented in [Appendix A](#).

4.1.1 Study Population

The study will enroll subjects who are ≥ 18 years of age with a known diagnosis of DM and fulfill one or both of the following criteria for DM:

- a. Bohan and Peter's criteria for probable or definite DM ([Bohan and Peter, 1975a](#); [Bohan and Peter 1975b](#))
- b. American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Myositis Response Criteria ([Lundberg et al, 2017](#)) criteria for idiopathic inflammatory myopathy and subclassified as amyopathic dermatomyositis (ADM), DM, juvenile-onset ADM, or juvenile-onset DM

and who also meet one of the following three criteria:

- a. Physician Global Assessment (MDGA) ≥ 3 cm (0 – 10 cm visual analogue scale or VAS) and manual muscle testing (MMT) of 8 muscle groups (MMT-8) score ≤ 142 (out of 150 total possible)
- b. Sum of MDGA, Patient Global Assessment (PtGA), and physician Extramuscular Global Assessment (EMGA) VAS scores ≥ 10 cm (all scores individually on 0-10 cm VAS)
- c. MDGA ≥ 3 cm and Cutaneous Dermatomyositis Activity and Severity Index (CDASI) activity score > 14

and who, if receiving these medications, are on:

- a. An unchanged dose of oral corticosteroids ≤ 20 mg per day or equivalent for ≥ 4 weeks before Visit 1
- b. Unchanged doses of immunosuppressive therapies (IST) other than corticosteroids for ≥ 8 weeks before Screening.

A complete list of the inclusion and exclusion criteria can be found in the study protocol.

4.1.2 Blinding

Dosing will be done in a double-blinded, randomized, placebo-controlled manner.

Lenabasum 5 mg and 20 mg and placebo capsules have similar physical appearance and will be packaged, labeled, and handled so that subjects and study staff are not able to distinguish among them. Identical assessments and procedures will be followed during the study for subjects assigned to lenabasum and placebo study groups.

All study subjects and the site study staff, including the investigators who will do safety and clinical assessments, qualified designees, study nurses, and study coordinators at the sites, will remain blinded to treatment assignment during the entire study, until the database is locked. If the treatment allocation for a subject otherwise becomes known to the investigator or other study staff at the site before database lock, the principal investigator or designee must notify Corbus immediately.

In an identical manner, all Corbus medical and clinical operations staff associated with the conduct of this study will remain blinded to treatment assignment during the entire study, until the database is locked.

Corbus clinical supplies personnel will be unblinded to the study product randomization. They are required not to reveal randomization information to others, unless a formal unblinded of information for a given subject is undertaken for safety reasons.

A limited number of contract laboratory personnel who perform and interpret assays of lenabasum concentrations and metabolites will be unblinded. Certain data management, programming, biostatistician, PK, Data Monitoring Committee members (DMC), and pharmacovigilance study personnel may be unblinded. These unblinded personnel will not be associated with the clinical conduct of the study and will not reveal to any clinical personnel involved in the study the treatment to which a subject is assigned.

4.1.3 Treatment Allocation

Subjects will be randomized centrally before or at Visit 1, with stratification by MMT-8 score (< 135 or ≥ 135), prednisone dose (≤ 10 mg or > 10 mg per day or equivalent) and by location of site (United States, non-United States). Subjects will be randomized and dosed at a ratio of 2:1:2 to lenabasum 20 mg, lenabasum 5 mg, or placebo arms using an Interactive Web-based Response System (IWRS) once a subject meets eligibility criteria and before first dose of study product.

4.1.4 Treatment Groups

Treatment groups are:

- Cohort 1: Lenabasum 20 mg BID
- Cohort 2: Lenabasum 5 mg BID
- Cohort 3: Placebo BID

4.1.5 Coronavirus Disease 2019 (COVID-19)

Starting in winter 2019/2020, a pandemic of infection with a new coronavirus (2019-nCoV) caused national and regional governments to restrict travel and gatherings of multiple people. Clinical study subjects' access to study sites and staff was severely restricted from mid-March 2020, as was study monitor access to on-site study data, and remains restricted at the time of writing this SAP.

The Sponsor developed and communicated a plan to manage safety and efficacy analyses of study subjects and maintain continuity of supply of study product to subjects, which is consistent with the *FDA Guidance on Conduct of Clinical Trials of Medical Products During COVID-19 Public Health Emergency* (FDA COVID-19 Conduct Guidance, March 2020). This plan was communicated to sites during a series of webcasts in March 2020, just before most restrictions began to take effect. As the Sponsor's management of the impact of COVID-19 evolved, any changes to the plan were communicated to the sites through e-mail or phone calls. The plan was communicated to internal study staff, vendor staff, study site

staff, and the DMC. Details of the plan and communication are maintained separately at Corbus.

Approaches to mitigating the potential major impact of COVID-19 on the performance of study JBT101-DM-002 are summarized in **Table 1**.

TABLE 1: Summary of Mitigation of Potential Negative Effects of COVID-19 on Study JBT101-DM-002

Potential negative effects of COVID-19 pandemic on execution of study JBT101-DM-002	Mitigation
<p>Subjects not able to have study visit at site because site is closed, site staff can't travel, or subject is at high risk during travel to site</p> <ul style="list-style-type: none"> • Missed visits • Visits outside study window • No safety assessment on site • Missed efficacy assessments • Subjects unable to get study product at site • Subjects need to make unscheduled visits to get or return study product 	<p>Extend visit windows by 1 week, to ± 2 weeks, to increase opportunity for study visits at site and full study evaluation</p> <p>Obtain safety follow-up using interview-based safety assessments over the phone or computer, between subjects and physicians. Document treatment-emergent adverse events (TEAEs) per protocol</p> <p>Obtain safety lab follow-up at local laboratories when possible. Results will be reviewed by study staff, put into source documents, but not study database</p> <p>To maintain continuity of dosing with study product:</p> <ul style="list-style-type: none"> • Make provisions for sites to ship study product directly to subjects. Obtain a Drug Enforcement Agency waiver for lenabasum so US sites can ship study product directly to subjects • Allow subjects to wait to return unused study product to site until end of study and to use that study product if needed to maintain continuity of dosing • Maintain subjects on a reduced dose of study product if direct shipment of study product to subject will not arrive in time to allow subject to continue to take full dose of study product. This approach is preferred to continuing subject on full dose of study product, then temporarily discontinuing study product altogether while waiting for direct shipment of study product to subject to arrive

	<ul style="list-style-type: none"> Allow subjects to pick-up or return study product at unscheduled visits if needed
Study staff not on site or have restricted access to site to enter study data. <ul style="list-style-type: none"> Late data entry Incomplete data entry 	Closely monitor site visits and data entry to determine what data will be late versus what will not be obtained. Work with sites to get data entered whenever possible
External monitors unable to travel to or enter study site to monitor data <ul style="list-style-type: none"> 100% source document verification will not be possible 	Remote data monitoring, as allowed by site/country policies Central data monitoring when data cannot be verified on site or by remote monitoring. Perform and document oversight of central data monitoring Resume source document verification on site when travel restrictions and access allow

Treatment assignment does not influence the negative effects of COVID-19 on execution of study JBT101-DM-002 or the plans put into place to mitigate those effects. The COVID-19 pandemic is not expected to introduce bias into the statistical analyses of the data.

A table listing changes to study plans to ensure continuity and oversight of the study will be included in the JBT101-DM-002 CSR.

A listing by subject and a table summarizing COVID-19 associated events by individual treatment cohorts and the combined lenabasum group will be provided. This listing and table will include protocol deviations.

Protocol deviations related to COVID-19 are expected to fall mostly into categories of study visits outside of windows, missing efficacy and safety assessments, and short periods of temporary reduction/discontinuation of study product.

Safety oversight was maintained throughout either with onsite visits or with interview-based safety assessments by the treating physician.

As identified to date, the effects of COVID-19 on subject disposition are:

- No subjects early terminated because of COVID-19
- All subjects had safety follow-up during COVID-19

The adjustments in this SAP for COVID-19-associated events are listed below and only apply when the event was related to COVID-19. None of the approaches are expected to introduce bias into the results missing efficacy assessments, because of COVID-19 is unrelated to treatment assignment.

FDA COVID-19 Statistical Guidance, June 2020:

- Protocol deviations will be identified as COVID-19-related

- Adverse events will be identified as COVID-19-related
- Concomitant medications given for COVID-19 associated illnesses will be identified as COVID-19-related
- Reduction in dose or interruptions in study product will be identified as COVID-19-related
- Safety laboratory test results done at local laboratories will not be included
- Early or late safety and efficacy assessments that are done out of window due to COVID-19 will be included as observed values
- Last post-Baseline observation carried forward (LOCF) will be used for missing efficacy values at incomplete visits or missed visits due to COVID-19
 - All results calculated centrally will continue to be calculated centrally from the carried forward values, for example, TIS, MDGA, and Health Assessment Questionnaire – Disability Index (HAQ-DI)
- Vaccination will be captured as concomitant medication

4.2 Study Endpoints

4.2.1 Primary Efficacy Endpoint

The primary efficacy endpoint is TIS by the 2016 ACR/EULAR Myositis Response Criteria, comparing lenabasum 20 mg BID to placebo at Week 28.

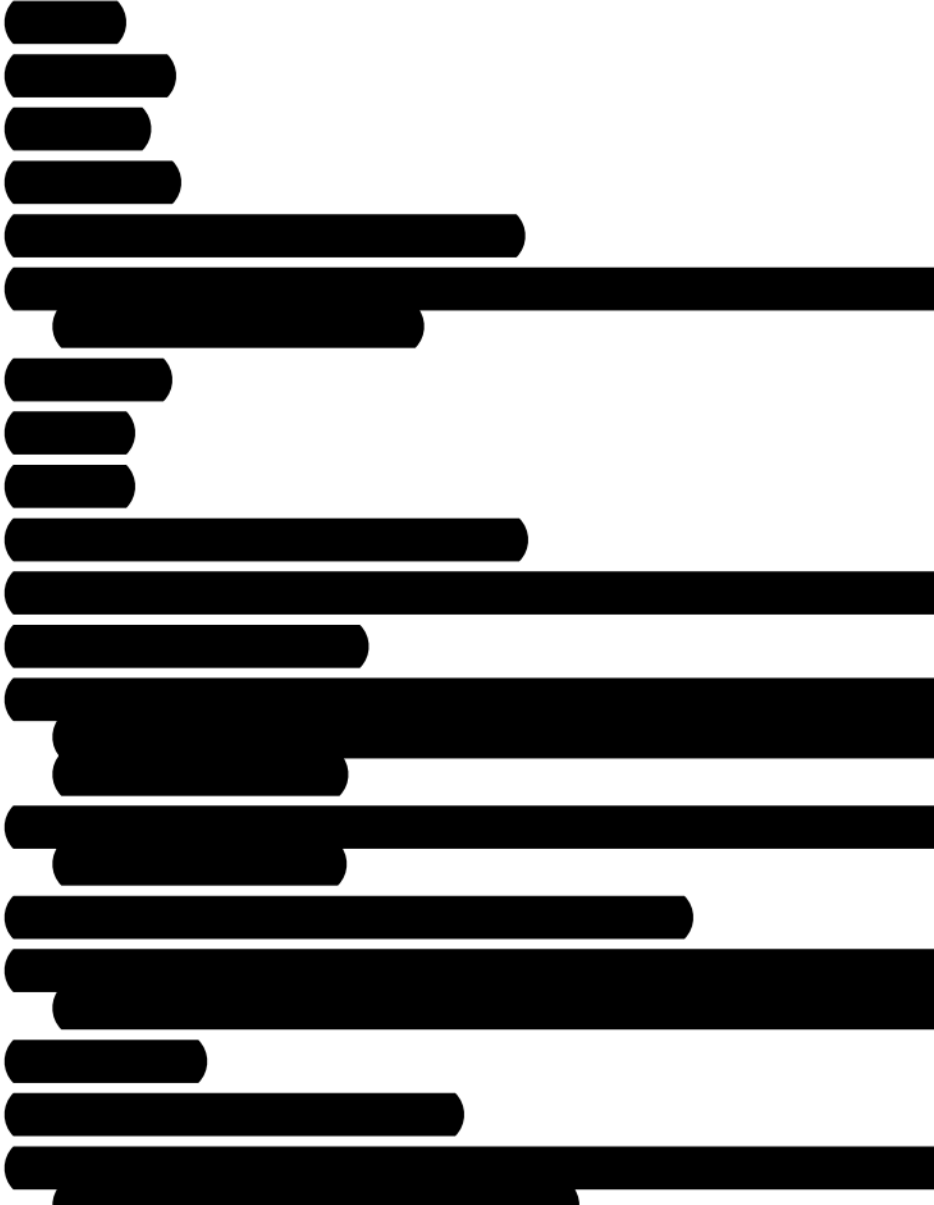
To support this composite primary efficacy endpoint, absolute value and change from Baseline in each of the 6 core set measures will be presented.

4.2.2 Secondary Efficacy Endpoints

The secondary efficacy endpoints include the following and are measured by the actual change from Baseline or proportion of subjects, for lenabasum compared to placebo at Week 28, unless otherwise specified:

- Subjects who achieve Definition of Improvement (DOI)
- Subjects who improve by at least one category on the Investigator Global Assessment (IGA) scale of skin activity
- CDASI activity score
- Subjects who achieve TIS ≥ 40 (at least moderate improvement)
- TIS in subjects receiving any IST (including corticosteroids) for > 1 year at Baseline
- Forced vital capacity (FVC) absolute change in L and percent predicted, in all subjects and those with interstitial lung disease (ILD) at Baseline. ILD is defined as a history of fibrosis on chest x-ray, a history of ILD on CT of lungs, and/or FVC % predicted $< 80\%$ at Screening or Visit 1
- TIS at Visit 10 (Week 52)
- TIS, lenabasum 5 mg BID versus placebo

4.2.3 Tertiary Efficacy Endpoints



[illegible]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

4.2.6 Pharmacokinetic Endpoints

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5 ASSESSMENT AND DERIVATION OF EFFICACY AND BIOMARKER ENDPOINTS

5.1 Primary Efficacy Variable

The primary efficacy endpoint will be the TIS by the 2016 ACR/EULAR Myositis Response Criteria, compared at Week 28 between lenabasum 20 mg BID and placebo groups. The TIS will be calculated centrally.

The ACR/EULAR TIS was developed and validated using expert consensus and data driven approaches for use in clinical trials and provides a broad comprehensive measure of improvement in disease activity (Aggarwal et al, 2017). Core set measures of myositis disease activity for adult DM/PM clinical trials have been established and validated by the International Myositis Assessment and Clinical Studies Group, and these measures were used as the foundation for the development of TIS.

Myositis response criteria were developed for both juvenile and adult populations and are based on a 0 – 100 scale. Six core measures are used to calculate the TIS (Aggarwal et al, 2017). Higher scores indicate better improvement in myositis symptoms.

The 6 core set measures that comprise the TIS are summarized below:

1. **MDGA:** An assessment of overall global disease activity by the physician will be done using a 10-cm VAS scale. The VAS scale is anchored by two verbal descriptors, “no disease activity” (score of 0) and “extremely active or severe disease activity” (score of 10). The physician will indicate the patient’s overall disease activity since the last visit by making a vertical mark on the scale. A higher score indicates worse
- [REDACTED]

overall disease activity. Additional detail and sample form can be found in [Appendix E](#). The physician assessments should ideally be done by the same investigator, and the physician should refer to subject's MDGA score from the previous visit to ensure consistency in rating. The MDGA will be calculated centrally.

2. **PtGA:** An assessment of overall global disease activity by the patient will be done using a 10-cm VAS. This VAS scale is anchored by 2 descriptors: "excellent" (score of 0) and "extremely poor" (score of 10). Subjects will assess their overall disease activity by drawing a vertical mark on a 0-10 cm VAS scale that best reflects their overall disease activity. The recall period is compared to the last visit. A higher score indicates worse overall health. Refer to [Appendix F](#) for sample questionnaire. The PtGA will be calculated centrally.
3. **MMT-8:** For the MMT-8 assessment, strength in the following 7 muscle groups will be assessed bilaterally and results recorded using a 0-10 point scale: deltoid, biceps, wrist extensors, gluteus maximus, gluteus medius, quadriceps, ankle dorsiflexors. An eighth muscle group, the neck flexors will also be assessed for strength using the 10-point scale. The MMT-8 score is the sum of all the bilateral muscle strength scores plus the neck flexor strength score, with a possible range from 0 - 150, with a score of 150 indicating normal muscle strength. A higher score indicates better muscle strength. The MMT-8 will be calculated centrally. See [Appendix C](#) for a sample MMT-8 form.
4. **HAQ-DI:** The HAQ-DI provides a patient-reported assessment of functional disability and includes 8 sections: dressing, arising, eating, walking, hygiene, reach, grip, and activities. There are 2 to 3 questions for each section; the recall period is 1 week. Scoring within each section is from 0 (without any difficulty) to 3 (unable to do). Scores are adjusted for use of aides, devices, or help from others. For the HAQ-DI, the score of each individual section is the highest score in that section. The HAQ-DI score will be calculated centrally. Specific details for calculating the HAQ-DI is found in [Appendix D](#). A higher total score indicates more functional disability. A pain score is also included in the HAQ.
5. **Most abnormal muscle enzymes:** The serum activities of the following muscle-associated enzymes will be assessed: alanine aminotransferase (ALT), asparagine aminotransferase (AST), lactic dehydrogenase (LDH), creatine kinase (CK), and aldolase. All muscle enzymes will be done at a central laboratory. The AST, ALT and LDH values will be done as part of the metabolic panel and CK and aldolase will be measured as additional muscle enzymes. The most abnormal muscle enzyme test among ALT, AST, LDH, CK and aldolase will be identified at Baseline [i.e., the test with highest value of actual value divided by the respective upper limit of normal range (ULN)] for each individual subject and used in the calculations of the TIS at subsequent visits. All muscle enzymes will be done at a central laboratory. The most abnormal muscle enzyme and change in muscle enzymes will be calculated centrally. Only muscle enzyme values that are abnormally high at Baseline (> ULN) will be included in assessing improvement from Baseline, for both the TIS and DOI.
6. **EMGA:** The EMGA encompasses an overall assessment of the disease activity in all the extramuscular organ systems and excludes muscle disease activity. EMGA will be

assessed by drawing a vertical mark on a 0-10 cm VAS scale. Anchored at each end of the 10-cm VAS are the descriptors “absent” (score of 0) and “maximum” (score of 10). The EMGA will be calculated centrally. Sample VAS questionnaire can be found in [Appendix G](#).

To calculate the TIS, the absolute percent change ($[\text{Final Value} - \text{Baseline Value}] / \text{Range} \times 100$) is first calculated for each of the 6 core measures described above. The ranges for MDGA, PtGA, MMT-8, HAQ-DI and EMGA are based on the instrument scale used (i.e., 10 for VAS scales, 150 for MMT-8, and 3 for HAQ-DI).

The range used for muscle enzymes will be based on which enzyme value is found to be the most abnormally high ($> \text{ULN}$) at Baseline: for creatine kinase, the range is 15x ULN, for aldolase, 6x ULN, and for ALT, AST and LDH, 3x ULN.

Based on the absolute percent change for each core measure, an improvement score will be assigned as shown in the table below. These individual improvement scores will then be summed to calculate the TIS. A TIS between 0 and 100 corresponds to the degree of improvement with higher scores indicating greater improvement.

Table 1. Algorithm to Calculate Total Improvement Score (TIS)

Conjoint analysis-based continuous response criteria using absolute percentage change in core set measures		
Core set measure	Level of Improvement	Level score
Physician Global Activity (MDGA)	Worsening to 5% improvement	0
	>5% to 15% improvement	7.5
	>15% to 25% improvement	15
	>25% to 40% improvement	17.5
	>40% improvement	20
Patient Global Activity (PtGA)	Worsening to 5% improvement	0
	>5% to 15% improvement	2.5
	>15% to 25% improvement	5
	>25% to 40% improvement	7.5
	>40% improvement	10
Manual Muscle Testing (MMT)	Worsening to 2% improvement	0
	>2% to 10% improvement	10
	>10% to 20% improvement	20
	>20% to 30% improvement	27.5
	>30% improvement	32.5
Health Assessment Questionnaire (HAQ)	Worsening to 5% improvement	0
	>5% to 15% improvement	5
	>15% to 25% improvement	7.5
	>25% to 40% improvement	7.5
	>40% improvement	10
Muscle Enzyme (most abnormal)	Worsening to 5% improvement	0
	>5% to 15% improvement	2.5
	>15% to 25% improvement	5
	>25% to 40% improvement	7.5
	>40% improvement	7.5
Extra muscular activity (EMGA)	Worsening to 5% improvement	0
	>5% to 15% improvement	7.5
	>15% to 25% improvement	12.5
	>25% to 40% improvement	15
	>40% improvement	20

It is important to note that when assigning the “level of improvement” that the direction of the test be considered, e.g., a negative percentage change is considered an improvement for PtGA, but not for MMT-8.

The LOCF approach can be used for 1-2 missing core set measures, but if more than 2 core set measures are missing, the TIS will not be calculated for that visit, with the exception of the stated convention for values/visits missing because of COVID-19 ([Section 5.13.1](#)).

In addition to the continuous TIS measure (0-100), categories for improvement were also developed ([Aggarwal et al, 2017](#)): a score ≥ 20 represents at least minimal improvement, a score of ≥ 40 represents at least moderate improvement and a score of ≥ 60 represents major improvement.

5.2 Secondary Efficacy Variables

5.2.1 Definition of Improvement

The DOI ([Oddis et al, 2013](#); [Rider et al, 2004](#)) is $\geq 20\%$ improvement in 3 of any 6 core set measures (same core set measures as used to determine the TIS), with no more than 2 core set measures worsening by $\geq 25\%$. Note that MMT-8 cannot be one of the worsening measures (i.e., for DOI to be achieved, MMT-8 cannot worsen by $\geq 25\%$). For improvement in muscle enzymes to contribute to DOI, the most abnormal muscle enzyme value must be greater than ULN at Baseline. The LOCF approach can be used for 1-2 missing core set measures, but if more than 2 core set measures are missing, the DOI will not be calculated for that visit, except for the convention for missing visits/values because of COVID-19 ([Section 5.13.1](#)).

5.2.2 Investigator Global Assessment Scale of Skin Activity

The IGA is a 5-point scale to evaluate overall skin activity by the investigator. Skin activity will be assessed as clear, almost clear, mild, moderate, or severe based on the overall description of each category as provided in [Appendix I](#).

5.2.3 Cutaneous Dermatomyositis Disease Area and Severity Index

The CDASI is a validated outcome measure that systematically quantifies cutaneous DM disease activity and damage ([Klein et al, 2007](#); [Yassaee et al, 2010](#)). In the CDASI activity score, DM skin disease activity is evaluated based on the physician's/qualified health personnel evaluation of erythema, scale, and erosion or ulceration at fifteen anatomic locations as well as alopecia, Gottron's sign or papules on the hands, and periungual changes. CDASI also includes a damage score. Both CDASI activity and damage scores will be calculated centrally.

Refer to [Appendix H](#) for the questionnaire and CDASI activity and damage score calculations.

5.2.4 Forced Vital Capacity

Spirometry to measure FVC (actual and % predicted values) will be done using equipment supplied by the Sponsor. Study staff will be trained in the proper use of the spirometry equipment. As possible, the same operator should record spirometry for a given subject. FVC values will be measured and calculated in compliance with American Thoracic Society standards for spirometry ([Miller et al, 2005](#)). Hankinson's reference values ([Hankinson et al, 2010](#)) will be used to determine FVC percent prediction with additional correction for Asian subjects. FVC values will be calculated centrally. A higher score indicates better lung function.

5.3 Tertiary Efficacy Variables

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[illegible]

[REDACTED]
 [REDACTED]
 [REDACTED]
 [REDACTED]
 [REDACTED]

[REDACTED]

- [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5.4 General Statistical Considerations

5.4.1 Reporting Conventions

The following reporting conventions will be used:

- Data from all study centers will be combined for analysis
- All data will be provided in data listings sorted by randomized cohort. The study center, subject number, age, sex, race, and visit will be presented in all listings, when applicable
- Descriptive statistics include: mean, median, standard deviation (SD), minimum (Min), maximum (Max), and n. Unless specified in the actual table shells, the mean, median, the upper and lower limits of the confidence interval will be displayed to one more decimal place than the original data (derived analysis data). The SD and standard error values will be displayed to two more decimal places than the original data. The minimum and maximum will be displayed to the same number of decimal places as the original data
- The number and percentage of responses will be presented in the form XX (XX.X%), where the percentage is in parentheses. The denominator of all percentages will be number of subjects in the analysis population, unless otherwise stated. When count data are presented, the percent will be suppressed when the count is zero to draw attention to the non-zero counts. A row denoted “Missing” will be included in count tabulations where necessary to account for dropouts and missing values. Non-zero percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places
- The day of the first dose of study product will be defined as Day 1. All study days before Day 1 will be calculated as assessment date – first dose date of study product.

The study day on or post Day 1 will be calculated as assessment date - first dose date of study product + 1

- Baseline value will be defined as the last non-missing value on or before Visit 1 and prior to the first dose of study product
- Change from Baseline will be calculated as the value at the post-Baseline visit minus the Baseline value
- Differences between treatment groups will be calculated as lenabasum minus placebo
- Listings will be presented for all enrolled subjects unless otherwise specified
- All analyses will be conducted using SAS Version 9.4 or higher
- The modified intent-to-treat (mITT) population will be the primary population for the efficacy analyses. In addition, supportive analyses using the per protocol (PP) population will be conducted for the primary efficacy endpoint, only if the PP population is < 90% of the mITT population
- P-values for analyses of primary efficacy, secondary, and tertiary efficacy variables will be assessed at a two-sided $\alpha = 0.05$ level

5.5 Statistical Hypotheses

Primary Endpoint: TIS at Week 28

H₀: The difference in the TIS between the active group and placebo (lenabasum 20 mg BID – placebo) at Week 28 = 0.

H₁: The difference in the TIS between the active group and placebo (lenabasum 20 mg BID – placebo) at Week 28 $\neq 0$, with superiority of active to placebo claimed if the difference between the active group and placebo group > 0 , which indicates a greater improvement in the active group.

5.6 Sample Size

This study is powered to detect a significant difference between lenabasum 20 mg BID and placebo in the primary endpoint at a two-sided alpha level of 0.05. The sample size has been set to detect a difference of 15 or more points in the TIS between the two treatment groups. Given an SD of 20.0, two-sided 0.05 alpha level test, and estimated dropout rate of 20%, 60 subjects per group are needed to achieve 95% power to detect a significant difference.

5.7 Interim Analyses

The planned interim analysis to re-estimate the sample size for this study was performed based on a separate SAP, analyzing variability in the primary endpoint TIS with all aggregated data and last available value when approximately 75 subjects had completed at least Visit 2 (4 weeks) and at least approximately 30 subjects had completed Visit 6 (28 weeks) of the study. This interim analysis was performed based on the blinded overall TIS score to examine the variance of the TIS, to potentially increase the sample size to maintain the power of the study without any statistical adjustment to the alpha level required (type I error). The results of the interim analysis indicated that no increase in sample size was needed.

5.8 Analysis Populations

5.8.1 Modified Intent to Treat Population

The mITT population will consist of all randomized subjects who have received at least one dose of study product and had at least one post baseline efficacy assessment. Analysis of the mITT population will be used as the primary efficacy analyses and will analyze subjects under the treatment to which they were randomized, regardless of compliance with assigned treatment.

5.8.2 Per-Protocol Population

The PP population will consist of subjects in the mITT population who complete the study without major protocol violations deemed likely to affect the primary efficacy outcome. These deviations will be classified during a blinded deviation review meeting before unblinding the study. The PP population will be used for sensitivity analyses of the primary efficacy endpoint, including subjects under the treatment received, if the PP population is < 90% of the mITT population.

5.8.3 Safety Population

The safety population will consist of all subjects who received any study product. Analyses performed on the safety population will be according to the treatment actually received.

5.8.4 Pharmacokinetic Population

The PK population will consist of all subjects from the safety population whose PK data are adequate for the calculation of primary PK parameters. Inclusion in the PK population of subjects with missing data or protocol violations or inadequate dosing will be considered on a case-by-case basis. The PK population will be the analysis set used for all PK analyses.

5.9 Subject Disposition

The disposition of all subjects over the course of the trial will be presented by treatment group, combined lenabasum group, and all subjects, using number of subjects and percentages. All percentages will be based on the number of subjects randomized.

Information will be presented on subjects who were or had: screening failures; randomized; subjects randomized but not treated; in each analysis population; completed the study; prematurely discontinued from study product but not the study; and prematurely discontinued from study. The reasons for premature treatment discontinuation will also be summarized. The reasons for premature treatment discontinuation include any one of the following:

- Randomized, but not dosed with study product
- Lack of efficacy – withdrawal by subject
- Lack of efficacy – physician decision
- Physician decision – other
- Withdrawal of consent by subject

- Lost to follow-up
- Non-compliance with study
- Adverse event, with indication whether possible- or-probably-related to study product
- Death
- Pregnancy
- Study terminated by Sponsor
- Other

5.10 Protocol Deviations

Protocol deviations will be recorded in the Clinical Trial Management System. All protocol deviations will be reviewed during a blinded deviation review meeting before database lock to classify the deviations into various categories and determine if they are major or minor protocol deviations. COVID-19 related protocol deviations will be captured per FDA guidance.

Major protocol deviations for this study may include, but are not limited to, any one of the following:

- Failure to comply with acceptable Good Clinical Practice guidelines
- Failure to meet eligibility criteria
- Use of a prohibited concomitant medication
- Failure to query the subject about potential AEs at each visit
- Failure to obtain MMT-8, HAQ-DI, MDGA, PtGA, EMGA and muscle enzymes at Visits 1 or 6 or 10 if applicable, unless the subject is unable to be assessed for safety reasons, for example, hospitalization or withdrawal of consent or COVID-19-related remote visits

A minor or administrative protocol deviation is an excursion from the protocol that does not affect the scientific soundness of the research plan or the rights, safety, or welfare of human subjects. Examples of minor or administrative deviations could include: follow-up visits that occurred outside the protocol-required time frame because of the subject's schedule or blood samples obtained at times close to but not precisely at the time points specified in the protocol.

The number and percentage of subjects with protocol deviations will be summarized by deviation category and type (major/minor) for individual cohorts and the combined lenabasum group for the mITT population. Protocol deviations with the deviation type of "Major Protocol Violation" or "Minor Protocol Deviation" flagged will be presented in a listing.

5.11 Demographics, Baseline Characteristics, and Baseline IST Treatment

Demographic, Baseline characteristics, and Baseline IST will be presented for all subjects and separately for Japanese subjects, by individual cohorts and the combined lenabasum group, for the mITT, PP, and safety populations. These data will also be presented in listings.

5.11.1 Demographics and Baseline Characteristics

Baseline demographic data including age (years), sex, race, ethnicity, height (cm), weight (kg), and BMI (kg/m²) will be summarized in a table.

5.11.2 Baseline Disease Characteristics

Baseline disease characteristics will be summarized in 1 or more tables and include disease duration, the frequency and proportion of subjects who meet DM classification criteria by Bohan and Peter's criteria and classification by those criteria for "no", "possible", "probable" and "definite" DM. The frequency and proportion of subjects who meet classification criteria for idiopathic inflammatory myopathy by 2017 ACR/EULAR criteria and subject classification into ADM, DM, juvenile-onset ADM, juvenile-onset DM, or not DM subgroups will be provided. Baseline values for efficacy outcomes, including MMT-8, MDGA, PtGA, HAQ-DI, HAQ-DI pain score, most abnormal muscle enzymes, EMGA, IGA, CDASI activity and damage scores, FVC L and % predicted, SkinDex-28 domains, 5D-itch score, PROMIS-29 domains, EQ-5D, Patient Pain VAS, and FACIT-F will be provided.

5.11.3 Baseline Immunosuppressive Therapies

A summary table will present the frequency and proportion of subjects who are receiving no Baseline IST, any Baseline IST, any Baseline IST by IST Group, 1 Baseline IST, and ≥ 2 Baseline IST. See [Section 5.12.1](#) for definitions. The data will also be presented in a listing.

5.11.4 General Medical History

General medication history will be coded using Medical Dictionary for Regulatory Activities (Version 23.1). The number and percentage of subjects with any general medical history will be summarized overall and by coded system organ class and preferred term. A summary table will be presented for individual cohorts and the combined lenabasum group for the safety population. The data will also be presented in a listing.

5.11.5 Other Dermatomyositis Medical History

The following DM medical history will be summarized for mITT, PP, and safety populations in a table and presented in a listing:

- Months since diagnosis, calculated as: (first dose date of study product – date of diagnosis) + 1 / 30.437.
- Musculoskeletal history
 - Muscle pain (yes, no)
 - Proximal muscle weakness (yes, no)
 - Respiratory muscle weakness (yes, no)

- Muscle atrophy (yes, no)
 - Muscle enzyme elevation (yes, no)
 - Muscle biopsy consistent with DM (yes, no)
 - Joint pain, swelling or tenderness (yes, no)
- Skin history
 - DM rash (yes, no)
 - Gottron's papules (yes, no)
 - Calcinosis (yes, no)
 - Ulcers/erosions (yes, no)
 - Hair loss related to dermatomyositis in the last 6 months (yes, no)
 - Skin pain (yes, no)
 - Itch (yes, no)
 - Skin biopsy consistent with DM (yes, no)
- Pulmonary history
 - Pleuritic chest pain/pleural effusions (yes, no)
 - Dyspnea that limits activities of daily living (yes, no)
 - Fibrosis (on plain chest X-Ray) (yes, no)
 - Interstitial lung disease (on chest computed tomography [CT]) (yes, no)
 - Require continuous supplemental oxygen (yes, no)
 - Lowest FVC % predicted within the last 12 months
- Cardiovascular history
 - Raynaud's phenomenon (yes, no)
 - Pericarditis/pericardial effusion (yes, no)
 - Palpitations (yes, no)
 - Documented cardiac conduction defects (yes, no)
 - Diastolic function abnormal (yes, no)
 - Reduced left ventricular ejection fraction (yes, no)
- Gastrointestinal symptoms
 - Dry mouth (yes, no)
 - Dysphagia (yes, no)
 - Gastroesophageal reflux disease (yes, no)
- Constitutional symptoms

- Fatigue or malaise within the last 3 months (yes, no)
 - Unintentional weight loss > 5 lbs within the last 3 months (yes, no)
 - Unexplained fever > 38°C on 2 occasions, ≥ 1 week apart within the last 3 months (yes, no)
 - Insomnia (yes, no)
- Other DM history
 - Dry eyes (yes, no)
 - Other DM-related symptoms (yes, no)

5.12 Treatments and Medications

5.12.1 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary Global B3 (September 2020). Concomitant medications used during Part A treatment will include all medications given to subjects during the first dose date and last dose date of study product, inclusive, which are reported on the Concomitant Medications electronic Case Report Form.

Prior medications will include all medications used in the last 12 months before the first dose of study product.

Medications used during the safety follow-up after last dose date of Part A study product will be listed.

The number and percentage of subjects in the safety population taking prior, concomitant medications, and medications during safety follow-up will be summarized separately by Anatomical Therapeutic Chemical (ATC) Level 4 and preferred term separately. The data will be summarized overall for individual cohorts and the combined lenabasum group.

Concomitant medications will be presented in a listing and newly initiated medications will be flagged.

5.12.1.1 Starting, Stopping, or Changing Doses of Concomitant Immunosuppressive/Immunomodulating Therapies

5.12.1.1.1 Concomitant immunosuppressive/immunomodulating therapies

Immunosuppressive/ immunomodulating therapies (collective referred to as IST) will be identified at Baseline and during the treatment period using a medically reviewed list of coded terms. Any IST medication:

- Must be listed on the concomitant medication list
- Must be received by the subject at least once on or after Day 1 through the day before the subject discontinues study product prematurely, discontinues Part A prematurely, or completes Visit 10
- ATC Level-2 Term must include:

- o Antineoplastic agents
- o Corticosteroids for systemic use
- o Immune sera and immunoglobulin
- o Immunosuppressants
- o Other dermatological preparations
- Route must include: oral, IV, intramuscular, or subcutaneous route, except for other dermatologic preparations, for which only glucocorticoids (ATC4 code) and corticosteroids for systemic use (ATC2 code) given by transdermal route are included. All medications administered by cutaneous, intraarticular, ophthalmic, other, and topical routes are excluded.

5.12.1.1.2 Baseline IST

Baseline IST is any IST with start date on or before Baseline and listed as ongoing at Baseline.

5.12.1.1.3 Change in IST

Changes in IST are relative to Baseline.

New IST means the subject:

- Was not receiving this IST as a Baseline IST
- If the IST was administered by oral, intramuscular, subcutaneous, or transdermal route, received this IST at any dose for a > 30-day consecutive period after Baseline and before Visit 10
- If the IST was by administered IV route, received at least 1 dose of this IST after Baseline and before Visit 10

Increased IST means the subject:

- Was on this Baseline IST
- If the IST was administered by oral, intramuscular, subcutaneous, or transdermal route:
 - o Received this IST at any dose for > 30-day consecutive period before Baseline
 - o Received this IST at doses that were $\geq 50\%$ higher than Baseline dose for > 30-day consecutive period after Baseline
 - o The subject could receive different doses of this IST and still be considered to have Increased IST, if each dose during the > 30-day period of increased doses was $\geq 50\%$ higher than Baseline dose
- If IST administered was by IV route
 - o Was on this Baseline IST, with last dose ≤ 6 months before Baseline

- Received this IST with at least one dose $\geq 50\%$ higher than the Baseline dose, at least once after Baseline and before Visit 10

Stopped IST means the subject:

- Was on this Baseline IST
- If the IST was administered by oral, intramuscular, subcutaneous, or transdermal route:
 - Received this IST at any dose for > 30 -day consecutive period before Baseline
 - Stopped this IST after Baseline and before Visit 10 for > 30 -day consecutive period, with stop date provided in concomitant medication list
- If the IST was administered by IV route
 - Was on this Baseline IST, with last dose ≤ 6 months before Baseline
 - Stopped this IST after Baseline and before Visit 10, with stop date provided in concomitant medication list

Reduced IST means the subject:

- Was on this Baseline IST
- If the IST was administered by oral, intramuscular, subcutaneous, or transdermal route:
 - Received this IST at any dose for > 30 -day consecutive period before Day 1
 - Received this IST at doses that were $\geq 50\%$ lower than Baseline dose for > 30 -day consecutive period after Baseline
 - The subject could receive different doses of this IST and still be considered to have Reduced IST, if each dose during the > 30 -day period of increased doses was $\geq 50\%$ lower than Baseline dose
- If the IST was administered by IV route
 - Was on this Baseline IST, with last dose ≤ 6 months before Baseline
 - Received this IST at doses that were $\geq 50\%$ lower than Baseline dose, at least once after Baseline and before Visit 10

5.12.1.1.4 Conversion of Doses of Interchangeable IST

For purposes of determining increases or decreases in IST doses, certain IST will be considered interchangeable, with relative doses in parentheses:

- Mycophenolate mofetil (500 mg), mycophenolate sodium (360 mg), and mycophenolic acid (360 mg)
- Methotrexate (2.5 mg) and methotrexate sodium (2.5 mg)
- Betamethasone (0.8 mg), cortisone (25 mg), deflazacort (6 mg), dexamethasone (0.8 mg), hydrocortisone (20 mg), methylprednisolone (4 mg), prednisolone (5 mg), prednisone (5 mg), and triamcinolone (4 mg)

5.12.1.1.5 Category of Change in IST and IST Groups

Subjects will be classified into 1 and only 1 category (listed below) of Change in IST category, based on the first day that requirements are met for any category of Change in IST. If a subject meets the requirements for ≥ 2 categories of Change in IST on the same day, the subject will be assigned to an IST category based on this order:

- No IST: Received no IST from Baseline through the day before Visit 10
- Stable IST: Received Baseline IST, and all Baseline IST were administered at stable doses from Baseline through discontinuation from Part A, either prematurely or at Visit 10.
- New IST: The subject received a New IST
- Increased IST: The subject received an Increased IST
- Stopped IST: The subject stopped a Baseline IST
- Decreased IST: The subject received a Decreased IST
- IST > 1 year which means if subject is on mycophenolate, IV immunoglobulin or oral corticosteroids, each must have treatment duration > 1 year. If the subject is not taking mycophenolate, IV immunoglobulin, or oral corticosteroids, but is on other Baseline IST, then at least 1 of the other IST must have treatment duration > 1 year

For purposes of describing subjects who are receiving similar IST in Tables and Listings, IST groups are defined as below:

- Mycophenolate: Mycophenolate mofetil, mycophenolate sodium, and mycophenolic acid
- Methotrexate: Methotrexate and methotrexate sodium
- Systemic corticosteroids: Betamethasone, cortisone, deflazacort, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, and triamcinolone
- Anti-malarials: Hydroxychloroquine, hydroxychloroquine sulfate, chloroquine, quinacrine
- IV immunoglobulin: immunoglobulin G human, immunoglobulin human normal, immunoglobulins NOS
- Azathioprine
- Monoclonal antibodies: Rituximab, adalimumab, ustekinumab
- Other immunosuppressive medications: Collective refers to all other IST, with reported names such as apremilast, baracitinib, ciclosporin, fluorouracil, leflunomide, mizorabine, tacrolimus, tacrolimus monohydrate, temozolomide, and tofacitinib citrate

5.12.1.1.6 Baseline IST by IST Treatment Duration

In some analyses, subjects will be grouped by no IST, IST ≤ 1 year treatment duration, and IST > 1 year treatment duration, with treatment duration as defined in [Section 5.12.1.1.5](#).

5.12.1.1.7 Summary of Baseline IST

See [Section 5.11.3](#). Numbers and proportions of subjects in individual cohorts and the combined lenabasum group who receive no Baseline IST, any Baseline IST, any Baseline IST by IST group ([Section 5.12.1.1.5](#)), 1 Baseline IST, and ≥ 2 Baseline IST will be provided.

5.12.1.1.8 Summary of Change in IST Categories

Frequency and proportion of subjects in individual cohorts and the combined lenabasum group who fall within different categories of Change in IST ([Section 5.12.1.1.5](#)) will be provided.

For the No IST and Stable IST categories, summaries will be provided of frequency and proportion of subjects in those categories who are taking different IST Groups ([Section 5.12.1.1.5](#)) at Baseline. For the New, Increased, Stopped, or Decreased IST Categories, summaries will be provided of frequency and proportion of subjects in those categories who started, increased, stopped, or decreased IST, respectively, by IST Group.

5.12.2 Study Treatments

5.12.2.1 Extent of Exposure

Duration of exposure to study product will be calculated as:

$$(\text{date of last dose} - \text{date of first dose}) + 1$$

Date of first dose is captured on the Study Drug Accountability electronic Case Report Form. Date of last dose is collected on the Study Termination electronic Case Report Form. For subjects missing last dose date or lost-to-follow-up, last dose date will be imputed using last visit date.

The duration of exposure will be summarized for individual cohorts and the combined lenabasum group.

All summaries will be based on the safety population.

5.12.2.2 Treatment Compliance

Study product compliance will be calculated for each subject by whether a subject takes all doses of study product as instructed. The number of capsules taken will be calculated by subtracting the number of capsules returned from the number of capsules dispensed for a given treatment period.

The study product compliance (%) will be calculated by dividing the total number of capsules taken by the total number of capsules prescribed and then multiplying by 100. For calculations of compliance, the number of capsules prescribed will be adjusted downward if the subject's study product was interrupted, as captured on the AE electronic Case Report Form.

$$\text{Compliance (\%)} = [(\text{no. of capsules dispensed} - \text{no. of capsules returned}) / (\text{no. of days in study for which capsules were prescribed} \times \text{no. of capsules prescribed per day})] \times 100$$

Study product compliance will be presented in a listing by individual and treatment cohort, with compliance presented as continuous variable. A subject will be considered compliant if the study product compliance is $\geq 80\%$ to $\leq 120\%$ of prescribed dose.

The overall study product compliance will be summarized by treatment cohorts and combined lenabasum cohort, with compliance presented as a continuous variable and as number of subjects and percentage of subjects in different categories of compliance ($< 80\%$, $80 - 120\%$, $> 120\%$).

5.13 Efficacy Analyses

5.13.1 Handling of Missing Data (Imputation Methods)

Analyses of the primary efficacy endpoint and secondary efficacy endpoints will impute missing data as follows:

- No missing data will be imputed for entire visits missed for reasons other than COVID-19
- For entire visits or entire primary or secondary efficacy outcome data that were missed because of COVID-19, efficacy data will be imputed using LOCF ([Section 4.1.5](#))
- For visits that were held and for which TIS core set measures are missing for reasons other than COVID-19, values for the TIS core set measures will be imputed using LOCF for ≤ 2 missing core set measures. If > 2 core set measures are missing, then TIS and DOI will not be calculated for that visit. In all cases, missing core set measures are to be imputed first, before the TIS and DOI are calculated. The TIS and DOI themselves will not be imputed.

5.13.2 Study Product and Study Discontinuation

Subjects who are permanently discontinued from study product for the study due to an AE related to study product will be followed until resolution or stabilization of the event. Subjects discontinued from study product or the study for any other reason except lost to follow-up will be evaluated through the time of their discontinuation from the study (regularly scheduled visit or an unscheduled visit). Unless consent is withdrawn or subject is lost to follow-up, subjects who permanently discontinue study product will be asked to return for safety and efficacy assessments at Visits 4, 6, 8, and 10 as applicable, starting with the next one of these visits that occurs after discontinuation of study product.

Data from subjects who discontinue study product, but remain in the study, will be included in data listings, but will not be included in summary statistics or analyses, with the exception of a sensitivity analysis for the primary endpoint.

Data from any early termination visit will not be included in efficacy analyses.

5.13.3 Adjustments for Multiplicity

The overall type I error rate will be controlled for primary and secondary outcomes with a hierarchical ordering of assessments. The order of the tests for treatment effect will be as follows:

- Primary efficacy outcome: TIS, lenabasum 20 mg BID versus placebo, at Week 28
- Secondary efficacy outcomes for lenabasum 20 mg BID versus placebo at Week 28, unless otherwise specified:
 - Proportion of subjects who achieve DOI
 - Proportion of subjects who improve by at least one category on the IGA scale of skin activity
 - CDASI activity score
 - Proportion of subjects who achieve TIS ≥ 40
 - TIS in subjects receiving IST for > 1 year at Baseline
 - FVC, absolute change in L and percent predicted, in all subjects and those with ILD at Baseline
 - TIS at Week 52
 - TIS, lenabasum 5 mg BID versus placebo

Secondary analyses will first compare lenabasum 20 mg BID to placebo, then compare lenabasum 5 mg BID to placebo, starting with TIS. Note that statistical significance for each endpoint must first be achieved in order to continue in the assessment of the next endpoint, following the testing sequence above.

5.13.4 Primary Efficacy Analysis

Primary analysis

The TIS will be summarized descriptively at each visit. The primary efficacy analysis is to compare the TIS at Week 28 between the lenabasum 20 mg BID and placebo groups using an MMRM. TIS scores in the lenabasum 20 mg BID and placebo cohorts will be compared at two-sided 0.05 level of significance. The model will have TIS score as a dependent variable, treatment, visit, treatment*visit interaction, gender (male, female), Baseline MMT-8 score (< 150 , 150), Baseline IST use [None, IST ≤ 1 year, IST > 1 year), Baseline IST*visit interaction, and region (United States, non-United States) as fixed factors, and subject as the repeated random effect. If any of the covariates do not significantly contribute to the model, they may be removed.

The TIS distribution will be assessed for normality. If the data do not meet the assumptions of normality, the MMRM model will be run using ranked values as the primary analysis.

Two-sided p-values and 95% CIs associated with the least-square mean difference between the lenabasum group and placebo will be presented for each visit. An unstructured covariance structure shared across treatment groups will be used to model the within-patient errors and the Kenward-Rogers correction to degrees of freedom will be applied. The focus of the model for the primary endpoint is the significance of the difference between lenabasum 20 mg BID and placebo at Week 28.

In case of difficulties with initially fitting the unstructured covariance matrix, alternative structures will be evaluated.

In addition, within-group change from Baseline will be assessed using paired t-tests.

Sensitivity Analysis

Sensitivity analyses on the primary endpoint will include repeating the primary analysis on the PP population if the PP population is < 90% of the mITT population and the following analyses on the mITT population:

- Subjects who discontinue study product or the study early for any reason other than early termination of the study by the Sponsor will be assigned a TIS score = 0 for all subsequent visits
- TIS is calculated only when all 6 core item scores are present
- Double-blind treatment completers only
- All missing data or visits are imputed using LOCF, where data after study product discontinuation are considered missing
- Analysis excluding: 1) subjects who meet the criteria for having an increase or decrease in IST, and 2) subjects with an increase in IST
- van Elteren test with factors for treatment, gender, Baseline MMT-8 score, Baseline IST use (yes, no), and region (United States, Non-United States). P-values for comparing treatment difference between lenabasum and placebo will be provided.
- 2-sample t-tests. P-values for comparing treatment difference between lenabasum and placebo will be provided.

Tipping-Point Approach

Tipping point analysis will be performed if the primary efficacy endpoint result is significant.

- Step 1: Calculate truly observed TIS scores. The TIS scores will be calculated only when all 6 core set measures are non-missing.
- Step 2: Impute missing TIS values with LOCF.
- Step 3: After obtaining imputed dataset in Step 2, we will shift TIS value x=1 in placebo cohort. Finally, we will get fully imputed datasets.
- Step 4: After obtaining fully imputed datasets in Step 3 perform the MMRM analysis using the actual TIS.
- The following SAS code will be used to compare treatment difference between lenabasum 20 mg BID and placebo.

```
ODS OUTPUT diffs=diffs;
PROC MIXED;
CLASS usubjid trtn region blmmtgr immugr sex visit;
MODEL aval = trtn visit region sex blmmtgr immugr
          trtn*visit immugr*visit/DDFM=KR;
REPEATED visit / SUBJECT=usubjid TYPE=un;
lsmeans trtn trtn*avisit/ cl diff;
```


RUN;

- Step 5: Repeat Steps 3 and 4 for each shift value, increasing the shift value from 1 to 2, 3, ..., until combined reference p-value > 0.05 . The actual shift values will be adjusted per data. The tipping point will be the shift value which causes the final test result to be reversed from significant to non-significant.

5.13.5 Secondary Efficacy Analyses

All summaries and analyses will be based on the mITT population.

Actual values at each visit and change from Baseline for each continuous secondary efficacy endpoint will be summarized for the comparisons and time points specified in [Section 4.2.2](#). Continuous secondary efficacy endpoints will be analyzed similarly to the primary MMRM model, using change from Baseline as the dependent variable, with the Baseline of each endpoint in the model to replace Baseline MMT-8, unless it is a TIS endpoint in which case Baseline MMT-8 will remain in the model.

In addition, categorical secondary efficacy endpoints will be summarized at each post-Baseline visit as actual values and proportion of subjects in each category, for the comparisons and time points specified in [Section 4.2.2](#). Data will be analyzed using Fisher's exact test or Cochran-Mantel-Haenszel tests stratified by the covariates used in the primary analysis model to test the treatment differences between lenabasum 20 mg BID and placebo cohorts at Week 28.

Secondary efficacy endpoints will be tested at a two-sided alpha level of 0.05.

5.13.7 Subgroup Analyses

Subgroup analyses of the primary efficacy endpoint based on the mITT population using data after missing data or visits due to COVID-19 are imputed using LOCF will be summarized and analyzed for various subgroups described in [Sections 5.13.4](#) and [5.13.5](#). Analysis methods will be similar to the analyses of corresponding primary or secondary efficacy endpoints described in [Sections 5.13.4](#) and [5.13.5](#).

5.13.8 Minimal Important Differences

The MID for an efficacy endpoint is defined as the smallest difference in a score of that measure that the patient will perceive as beneficial. The calculations of patient-

reported/physician-reported population MIDs for TIS, DOI, change in IGA, and change in CDASI activity score are provided in [Section 5.3.11](#) and [Section 5.3.12](#). The calculated MIDs will be summarized by patient-report/physician-report for each endpoint, for all subjects, individual cohorts, and the combined lenabasum group, at Visits, 4, 6, and 10, as applicable.

In addition, the proportion of subjects who achieve or do not achieve a MID level of improvement will be summarized for TIS, DOI, change in IGA, and change in CDASI activity score, for all subjects, individual cohorts, and the combined lenabasum group, at Visits, 4, 6, and 10.

5.14 Safety Analyses

Summaries of the safety data will be done using observed data using the safety population. No formal statistical testing will be performed to compare safety in different treatment groups.

All safety data will be presented in listings.

5.14.1 Adverse Events

AEs will be coded using Medical Dictionary for Regulatory Activities, Version 21.1.

Treatment-emergent AEs include all AEs onset between first dose and last dose of the study product, inclusive. Treatment-emergent AEs and AE onset during the 28-day follow-up will be summarized separately. Any AEs that occur before first dosing will be summarized in a table as Pre-Treatment AEs.

An overall summary by individual cohort and the combined lenabasum group will be presented that includes the number and proportions of subjects who experienced at least one TEAE, serious TEAE, TEAEs/serious TEAEs by maximum severity, TEAEs/serious TEAEs by strongest relationship to study product, TEAEs leading to premature study product discontinuation, probably- and definitely-related TEAEs leading to premature study product discontinuation, TEAEs leading to premature study discontinuation, probably- and definitely-related TEAEs leading to premature study discontinuation, TEAEs of abuse potential, and death.

The number and proportions of subjects with the TEAEs listed below will be summarized by System Organ Class (SOC), preferred term, and treatment separately. The total number of TEAEs by SOC and preferred term will also be presented. If a subject reports the same preferred term multiple times within the same SOC, that subject will only be counted once for the SOC. As with the preferred term, if a subject reports multiple conditions within the same preferred term, that subject will only be counted once for the preferred term.

- TEAEs
- Serious TEAEs
- TEAEs leading to premature study product discontinuation, overall and by those probably- and definitely-related to study product

- TEAEs leading to premature study discontinuation, overall and by those probably- and definitely-related to study product
- TEAEs by maximum severity
- TEAEs by strongest relationship to study product
- TEAEs by occurrence period (1 to 30 days, 31 to 90 days, 91 to 181 days, 182 to 272 days, > 272 days)
- TEAEs of abuse potential; relevant preferred terms include the following:
Anxiety, apathy, bradykinesia, bradyphrenia, cognitive disorder, confusional state, depressed level of consciousness, depressed mood, depression, derealization, disorientation, dissociation, disturbance in attention, dizziness, dyskinesia, dysphoria, elevated mood, euphoric mood, feeling abnormal, feeling drunk, feeling jittery, feeling of relaxation, hallucination, hyperflexia, hypersomnia, hypoaesthesia, hypoflexia, inappropriate affect, insomnia, lethargy, malaise, mental disorder, mental impairment, mobility decreased, mood altered, nervous system disorder, nervousness, neuralgia, panic attack, paraesthesia, restlessness, sleep disorder, sluggishness, somnolence, stupor, thinking abnormal, vision blurred, visual disturbance, visual impairment, sensory disturbance, amnesia, irritability, memory impairment, agitation, and any other related terms

Similar to TEAEs tables, another set of tables for AEs that began during the 28-day safety follow-up period will be provided.

All AEs, serious adverse events, AEs leading to premature study product discontinuation, AEs leading to premature study discontinuation, fatal AEs, and AEs of abuse potential will be presented in listings separately.

5.14.2 Clinical Laboratory Evaluations

Hematology includes complete blood count with differential cell count and platelets.

Serum chemistry includes metabolic panel (at least glucose, urea nitrogen, creatinine, sodium, potassium, chloride, carbon dioxide, calcium, total protein, albumin, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase and gamma glutamyl transferase) and other tests (serum β human chorionic gonadotrophic hormone in women of childbearing potential, follicle stimulating hormone, human immunodeficiency virus screening test, and hepatitis B and C screening tests).

Urinalysis includes urine pregnancy tests for women of childbearing potential and urine dipstick for blood, albumin/protein, and glucose.

For the purposes of summarization in both the tables and listings, all laboratory values will be converted to standardized units. The actual values and changes from Baseline to each post-Baseline visit in each laboratory test with numeric results will be summarized for individual cohorts and the combined lenabasum group.

Laboratory test results will be classified as Low, Normal, and High, or Normal/Abnormal according to the normal ranges. These categorical data will be summarized in shift tables for

shift from Baseline to each post-Baseline visit for individual cohorts and the combined lenabasum group.

5.14.3 Vital Signs, Weight and BMI

Vital signs will include systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, and body temperature. Weight and height will also be measured, and BMI will be calculated.

The actual values, changes from Baseline to each post-Baseline visit in each vital sign parameter, weight, and BMI will be summarized for individual cohorts and the combined lenabasum group.

5.14.4 Physical Examinations

Physical examination (including brief examination) results will be presented in listing only. A listing of clinically significant abnormal results will also be provided.

5.14.5 Electrocardiograms

Electrocardiogram parameters include heart rate, RR interval, QRS duration, PR interval, QT interval, and QT interval correction by Fridericia's formula. In addition, ECG evaluation of abnormality and interpretive statements will also be reported.

The actual values and change from Baseline for every post-Baseline visit/time point in each ECG parameter will be summarized by treatment and visit/time point.

5.15 Biomarker Analyses

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5.16 Pharmacokinetic Analyses

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5.16.2 Analysis of Pharmacokinetic Endpoints

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

6 DATA MONITORING COMMITTEE

Oversight of subject safety in this trial will be provided by an independent unblinded DMC, which will advise Corbus and the site investigators. The voting members of the DMC will include at least three external experts in DM who will be supported by an unblinded biostatistician, who will be a non-voting member. A non-voting member may be added to provide clarifications and historical perspective, at least during Open Sessions of the DMC meeting. Additional experts in areas related to DM, safety, or regulatory requirements or practices can be added as needed.

The independent DMC will review the accumulated safety and operational data about every 6 months through the last subject last visit, or more frequently if necessary. The DMC will review interim/cumulative data for evidence of study-related AEs and factors external to the study such as scientific or therapeutic developments that may impact participant safety. The DMC will also review progress of the study and efficacy outcomes. The DMC may make recommendations to Corbus about any of the items it reviews.

The following outputs will be provided in blinded formats for the DMC review. Blinded versions will be provided by the lead statistician for discussion, and unblinded versions will be provided by the unblinded statistician for discussion upon request of the DMC.

The following tables will be generated based on the safety set for the DMC members:

- Subject disposition
- Demographics and baseline characteristics
- TEAEs by System Organ Class and Preferred Term
- TEAEs by System Organ Class, Preferred Term and strongest relationship to study product by treatment period

- Serious TEAEs by System Organ Class and Preferred Term

The following listings will be generated:

- Subject disposition
- TEAEs
- SAEs
- All AEs by relationship to study product
- Laboratory results - hematology
- Laboratory results - blood chemistry
- Laboratory results - urinalysis
- Vital signs, weight, and BMI
- ECG results

7 CHANGES IN PROTOCOL PLANNED ANALYSES

Changes or modifications from the planned analyses in the protocol include the following:

- The definition of the mITT population was clarified to include that subjects must have at least one follow-up efficacy assessment.
- The primary MMRM analysis model includes an additional factor for gender, and replaces prednisone with IST.
- CDASI activity score has been moved up in the hierarchical testing order of secondary efficacy endpoints, and FVC has been moved from the tertiary endpoints to the secondary endpoints.

8 REFERENCES

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9 APPENDICES

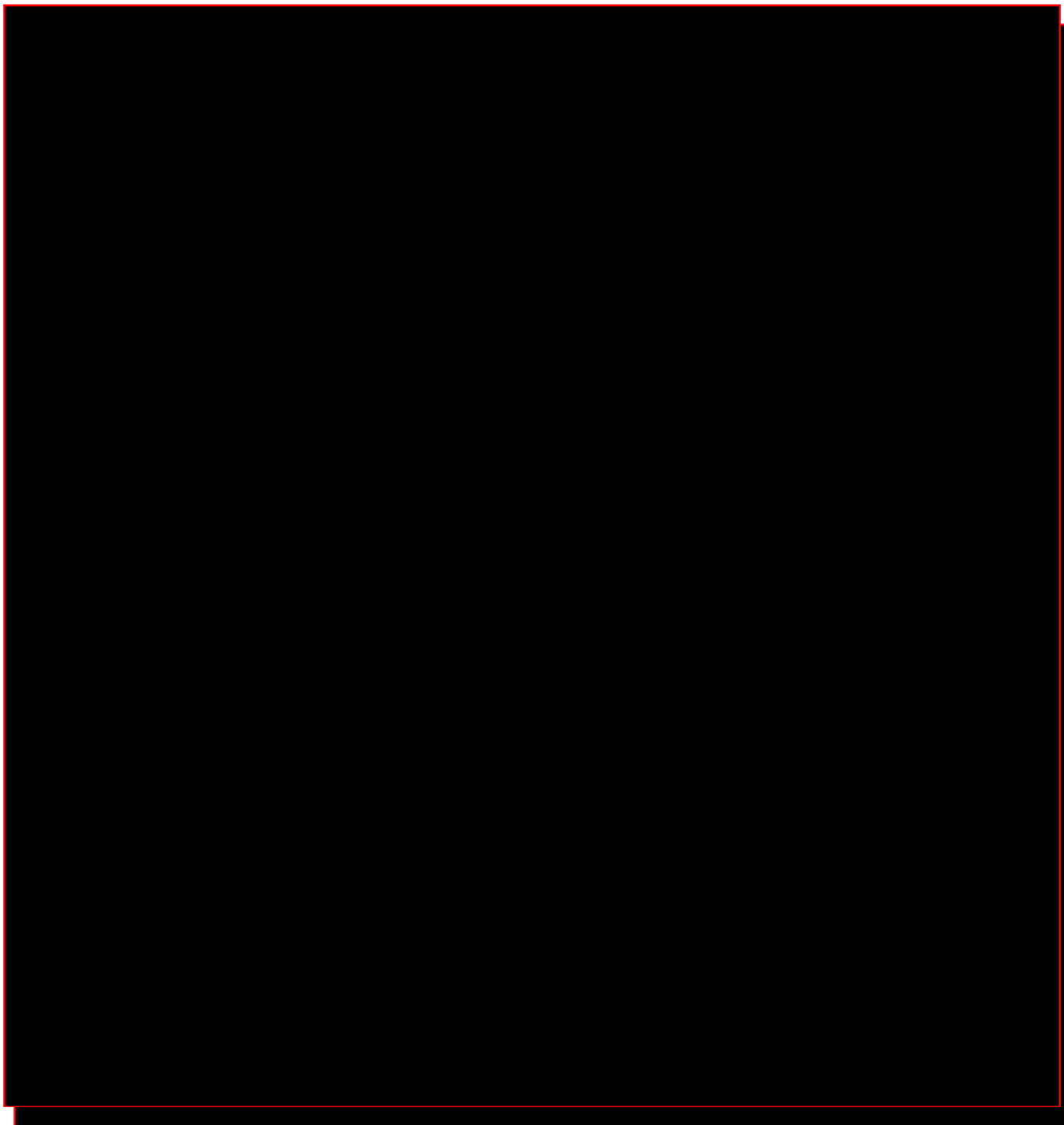
APPENDIX A: SCHEDULE OF STUDY PROCEDURES

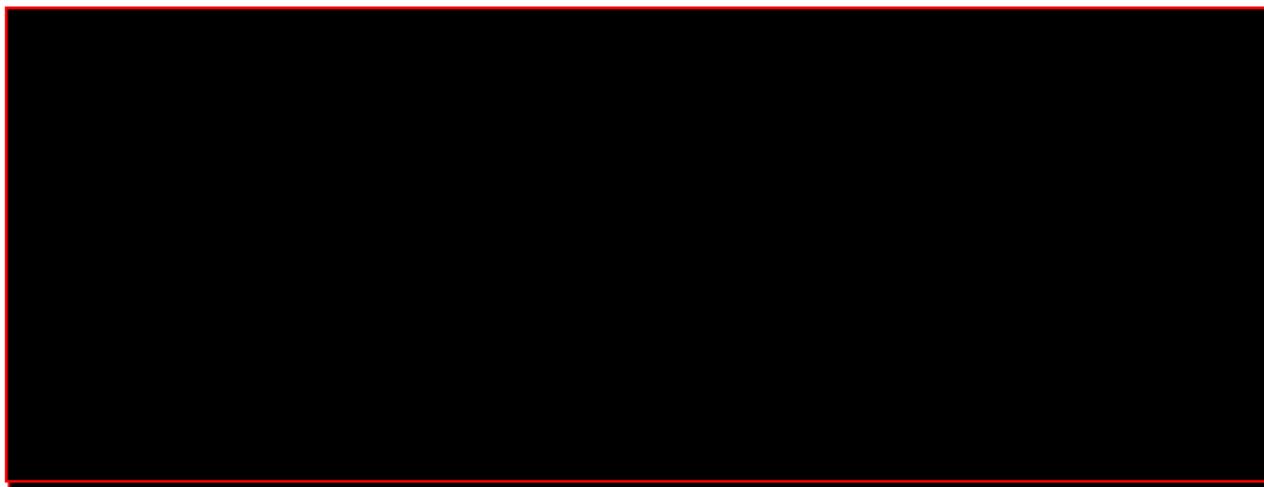
	Visit	Screening Up to -4	Treatment Period										ET	Follow - up ^x 4±1
	Week		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10		
			Day 1	4±1	10± 1	16± 1	22± 1	28± 1	34±1	40± 1	46± 1	52± 1		
ELIGIBILITY ASSESSMENTS														
Informed Consent		X										X ^w		
Eligibility criteria ^a		X	X											
Medical history ^b		X												
Physician assessment of DM activity		X												
Concomitant medications ^c		X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs ^d and weight ^e		X	X	X	X	X	X	X	X	X	X	X	X	X
Height ^f		X												
Full physical examination ^g		X	X									X	X	
Brief physical examination ^h				X	X	X	X	X	X	X	X			X
HIV, HBV and HCV testing		X												
FSH and LH ⁱ		X												
Contraceptive assessment ^j and record LMP for WOCBP		X	X	X	X	X	X	X	X	X	X	X	X	X
Serum β HCG for WOCBP		X												
Urine β HCG for WOCBP			X	X	X	X	X	X	X	X	X	X	X	X
SAFETY ASSESSMENTS														
AE monitoring		X ^k	X	X	X	X	X	X	X	X	X	X	X	X
12 lead ECG ^l		X	X	X				X				X	X	
Safety phone call to subject											X ^m			
RANDOMIZATION														
Randomization (IWRS) ⁿ			X											
STUDY PRODUCT ADMINISTRATION														
Administer study product in clinic			X ^o											
Dispense study product ^p			X	X	X	X	X	X	X	X	X			
Collect and count capsules of returned study product				X	X	X	X	X	X	X	X	X	X	
PtGA		X	X	X		X		X		X		X	X	
HAQ-DI		X	X	X		X		X		X		X	X	

	Visit	Screening Up to -4	Treatment Period										ET	Follow - up ^x 4±1
	Week		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10		
			Day 1	4±1	10± 1	16± 1	22± 1	28± 1	34±1	40± 1	46± 1	52± 1		
PATIENT-REPORTED EFFICACY ASSESSMENTS ^q														
SF-36		X	X	X		X		X		X		X	X	
PROMIS-29 Short Form		X	X	X		X		X		X		X	X	
Patient VAS score for pain		X	X	X		X		X		X		X	X	
FACIT-Fatigue Score		X	X	X		X		X		X		X	X	
5-D Itch Questionnaire		X	X	X		X		X		X		X	X	
Skindex-29+3		X	X	X		X		X		X		X	X	
EQ-5D questionnaire		X	X	X		X		X		X		X	X	
PHYSICIAN ASSESSMENTS OF EFFICACY ^r														
MMT-8		X	X	X		X		X		X		X	X	
CDASI score		X	X	X		X		X		X		X	X	
IGA scale of skin activity		X	X	X		X		X		X		X	X	
EMGA (10 cm VAS)		X	X	X		X		X		X		X	X	
MDGA (10-cm VAS and Likert Scale)		X	X	X		X		X		X		X	X	
LABORATORY ASSESSMENTS														
CBC with differential and platelets		X	X	X	X	X	X	X	X	X	X	X	X	X
Metabolic panel (includes ALT, AST and LDH) ^s		X	X	X	X	X	X	X	X	X	X	X	X	X
CK and aldolase		X	X	X		X		X		X		X	X	
Blood biomarkers			X					X				X	X	
Blood for flow cytometry (at selected sites)			X					X				X	X	
Paxgene tube collection			X									X	X	
Autoantibody measurements			X									X	X	
Urine dipstick ^t			X	X				X				X	X	
PHARMACOKINETIC ASSESSMENTS														
Lenabasum plasma concentration and metabolite profiling ^u			X	X		X		X				X	X	
ADDITIONAL ASSESSMENTS														
Spirometry		X	X			X		X				X	X	
Skin biopsies (optional at selected sites) ^v			X			X						X	X	
Skin photography (optional at selected sites)			X									X	X	
Patient Improvement Questionnaire for Subjects						X		X				X	X	
Patient Improvement Questionnaire for Physicians						X		X				X	X	

- ^a Must fulfill Bohan and Peter's criteria for probable or definite DM or ACR/EULAR criteria for DM
- ^b Medical history includes the following: subject demographic information, history and disease manifestations of DM including ILD, concurrent illnesses and past, smoking history (packyears) classified into one of the following categories: current smoker; ever smoked (≥ 1 cigarette/day for > 1 year); never smoked, and any other relevant medical history.
- ^c Doses of IST (including corticosteroids) should be assessed at every study visit along with all other concomitant medications.
- ^d Systolic and diastolic BP will be measured with the subject supine for at least 5 minutes. The same arm should be used for the measurement throughout the study as much as possible. Pulse and respiration will also be measured with the subject supine for at least 5 minutes. Body temperature will be measured on the skin or in the mouth.
- ^e Weight will be measured with coats, jacket, and footwear removed.
- ^f Standing height will be measured with footwear removed.
- ^g Full physical examination includes the following assessments: alertness and orientation, general appearance, skin, head, eyes, ears, nose, and throat, lungs, heart, abdomen, musculoskeletal examination, and lymph nodes. Breast and genitourinary examinations are not required.
- ^h Brief physical examination includes the following assessments: skin, lung, heart, abdomen, and any other area as indicated by changes in medical history.
- ⁱ Applicable for women ≤ 55 years of age with no menses for ≥ 1 year.
- ^j Refer to Protocol Appendix 1 for the criteria for determining reproductive potential and acceptable methods of contraception.
- ^k AE monitoring should begin at subject consent.
- ^l 12-lead ECG with QT/QTc intervals should be recorded with the subject in a rested supine position ≥ 10 minutes before the test.
- ^m Study personnel will be required to contact subjects 3 ± 1 week after Visit 9.
- ⁿ To occur at or before Visit 1.
- ^o The first dose of study product on Visit 1 will be taken in clinic from the dispensed study product. Vital signs include blood pressure, pulse rate, respiratory rate, and temperature and will be measured pre-dose and 3.0 ± 0.5 hours after administration of first dose of study product at Visit 1 in the clinic. ECGs will be recorded pre-dose and 3.0 ± 0.5 hours after administration of first dose of study product in the clinic.
- ^p Study product will be dispensed for administration in WOCBP only if urine pregnancy test is negative.
- ^q Ideally, all patient-reported efficacy assessments should be completed before all other study procedures, in the order listed.
- ^r It is preferred that physician assessments of efficacy are performed in the order listed.
- ^s Metabolic panel includes glucose, urea nitrogen, creatinine, estimated glomerular filtration rate, blood urea nitrogen/creatinine, sodium, potassium, chloride, carbon dioxide, calcium, protein total, albumin, bilirubin total, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH); AST, ALT and LDH are three of the five muscle enzymes comprising the TIS (see Protocol Section 8.1.2).
- ^t Urine dipstick for blood, protein, glucose
- ^u Pharmacokinetic blood samples will be collected at Visit 1 pre-dose and 3.0 ± 0.5 hours after administration of first dose of study product in the clinic. Time of administration of the first study dose and time of PK sample collection (blood draw for PK) should be recorded At Visits 2, 4, 6, and 10, PK blood samples will be collected once during the visit and time of most recent dose of study product and blood collection should be recorded. Time of the blood draw should be 8-16 hours after the last dose of the study product, which typically would have been taken the evening before the visit.
- ^v Five optional, 4 mm skin biopsies will be collected: two at Visit 1, two at Visit 4 and one at Visit 10. At Site 1001, subjects will have the option to consent to two 6 mm and three 4 mm biopsies (e.g., one 4 mm and one 6 mm at Visit 1; one 4 mm and one 6 mm at Visit 4, and one 4 mm at Visit 10). Skin biopsies will only be conducted at selected sites.
- ^w Subjects who rollover into Part B should sign an ICF by Visit 10 and preferably earlier than Visit 10, if possible.
- ^x The Safety Follow-up Visit is to occur 4 ± 1 weeks after the last visit (V10/ET) and is to be completed by subjects who do not rollover into Part B.

APPENDIX B: IMPUTATION ALGORITHM FOR PARTIAL AND MISSING DATES

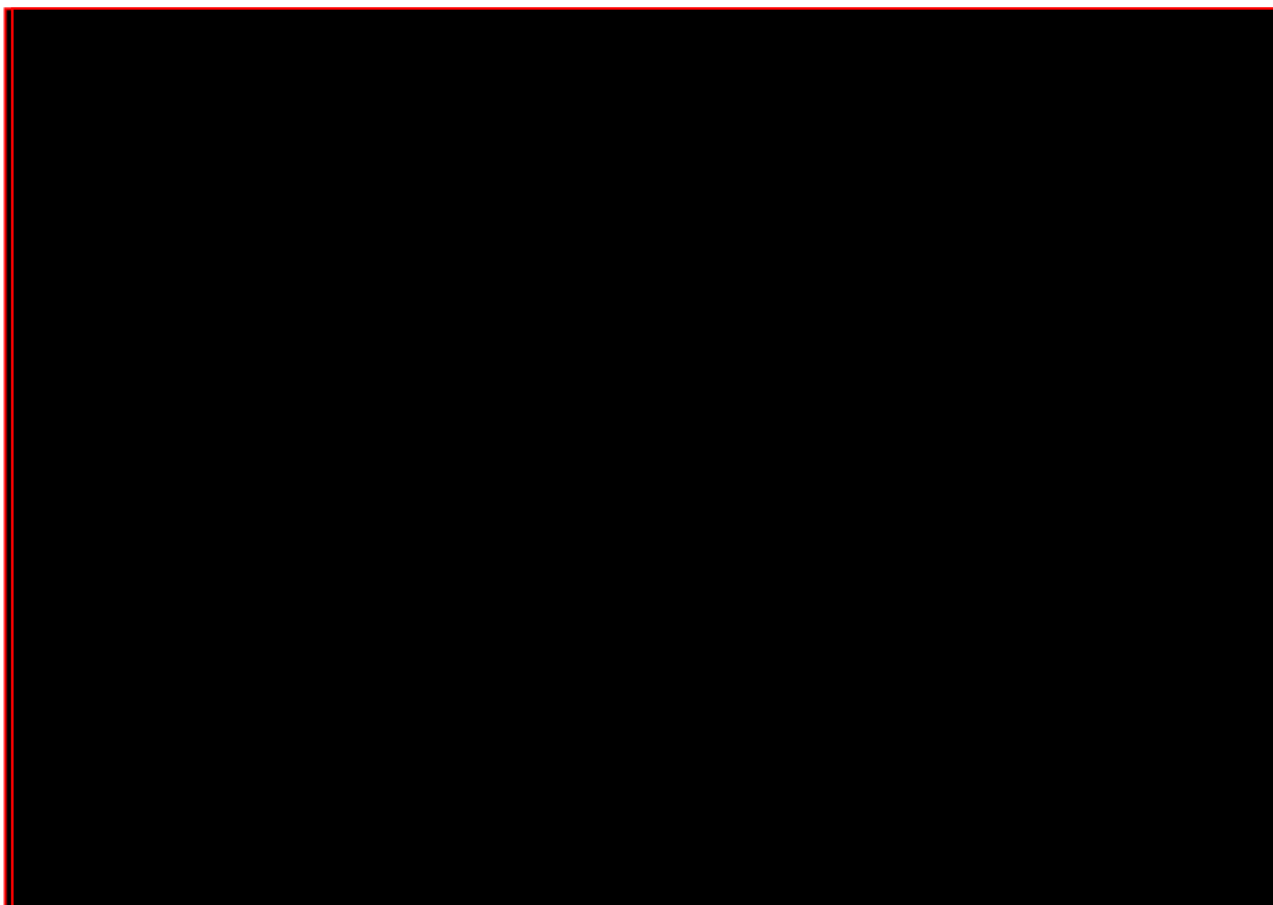




APPENDIX C: MANUAL MUSCLE TEST – 8 ITEMS



Key to Muscle Grading



APPENDIX D: HEALTH ASSESSMENT QUESTIONNAIRE-DISABILITY INDEX (HAQ-DI)

Health Assessment Questionnaire-Disability Index consists of 20-item disability scales as the following:

The diagram consists of a series of horizontal black bars of varying lengths, arranged in a sequence. Some bars have small black circles at their ends, suggesting a timeline or process flow. The bars are arranged in a way that suggests a sequence of events or steps, with some bars being longer than others, indicating different durations or stages. The overall structure is a series of connected horizontal segments, with some segments having small circles at their ends, possibly representing a timeline or a process flow.

[REDACTED]

- ☐ [REDACTED] ☐ [REDACTED]
☐ [REDACTED]
☐ [REDACTED]
☐ [REDACTED]

- ☐ _____
- ☐ _____

[illegible]

[illegible]

APPENDIX E: PHYSICIAN GLOBAL ASSESSMENT (MDGA)

[REDACTED]

•

[REDACTED]

•

[REDACTED]

•

____ - ____ cm

[REDACTED]

•

[REDACTED]

[REDACTED]

APPENDIX F: PATIENT GLOBAL ASSESSMENT (PTGA)

[REDACTED]

•

[REDACTED]

•

[REDACTED]

_____. _____. _____. cm

APPENDIX G: EXTRAMUSCULAR GLOBAL ASSESSMENT (EMGA)

[REDACTED]

•

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

•

[REDACTED]

[REDACTED]

APPENDIX H: CUTANEOUS DERMATOMYOSITIS DISEASE AREA AND SEVERITY INDEX (CDASI)

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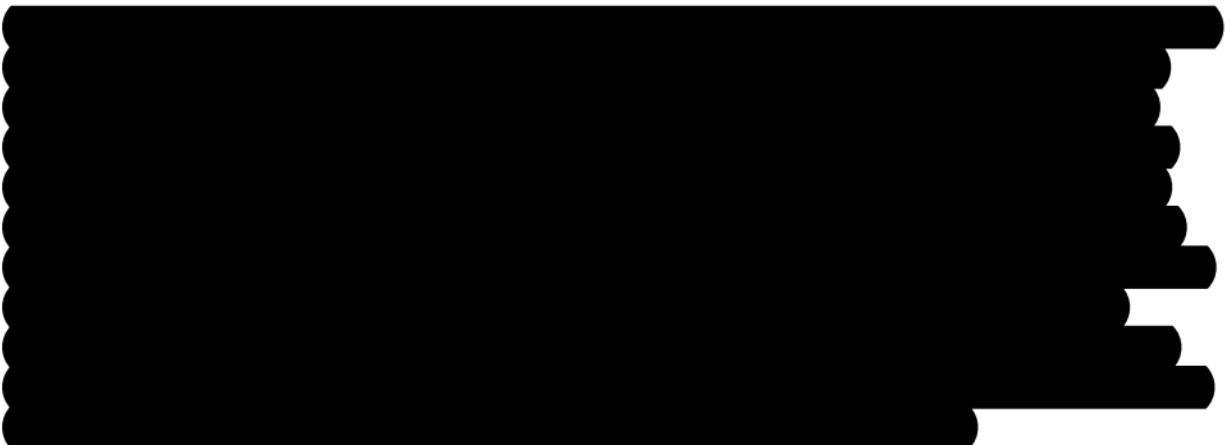
[illegible]

[REDACTED]

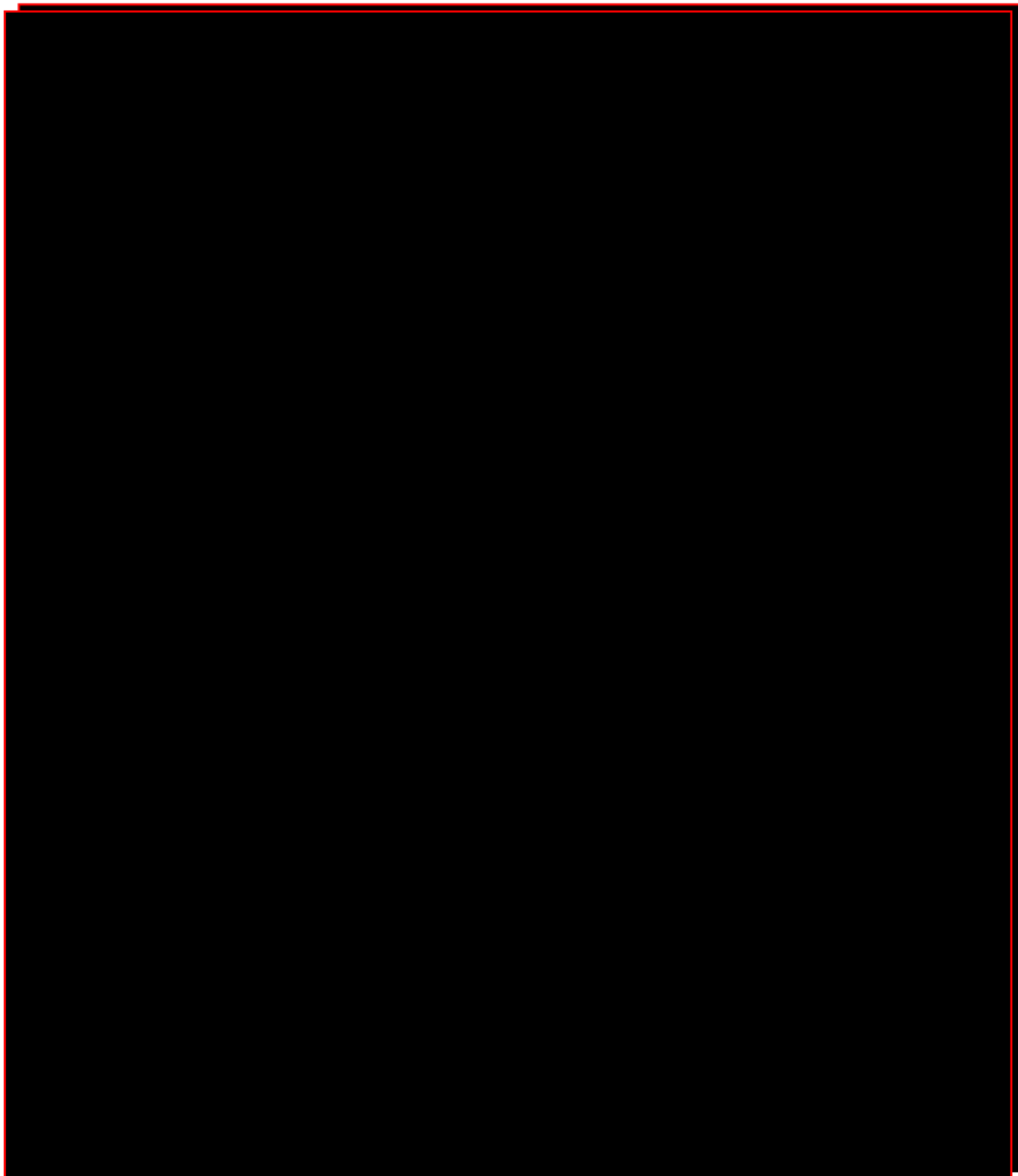
[REDACTED]

[illegible]

APPENDIX K: 5-DIMENSION ITCH QUESTIONNAIRE

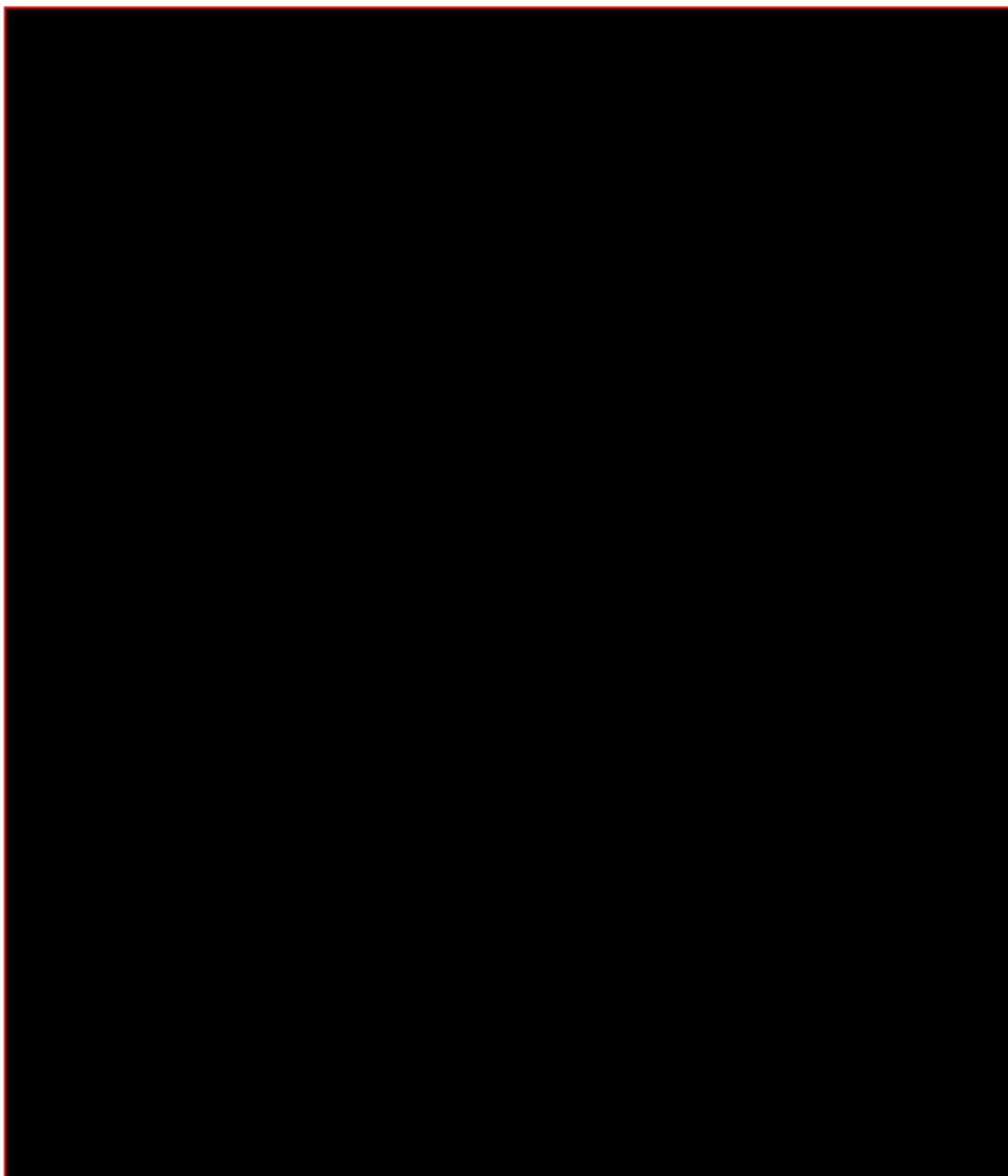


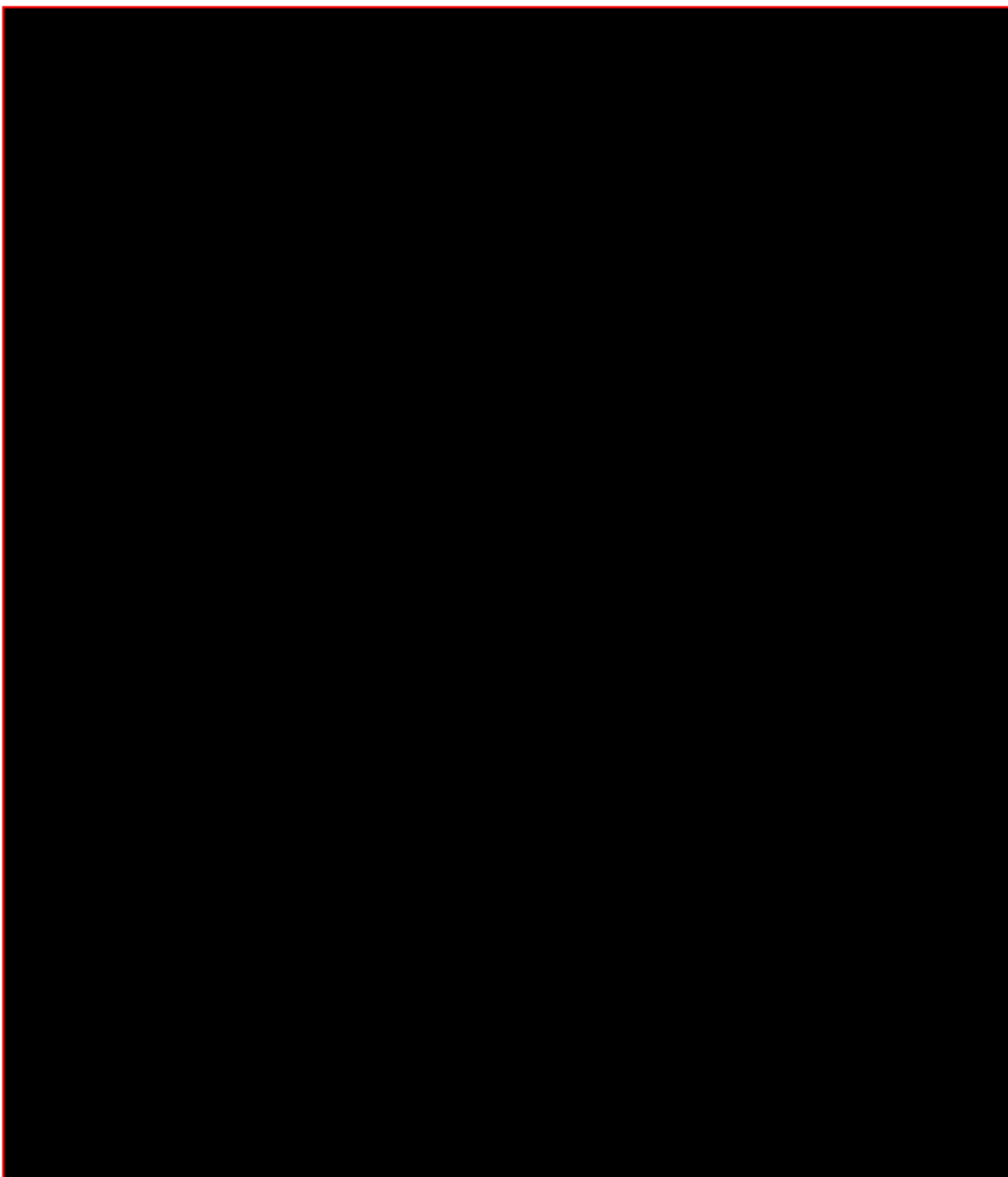
5-D Pruritus Scale



APPENDIX L: PROMIS-29 SHORT FORM

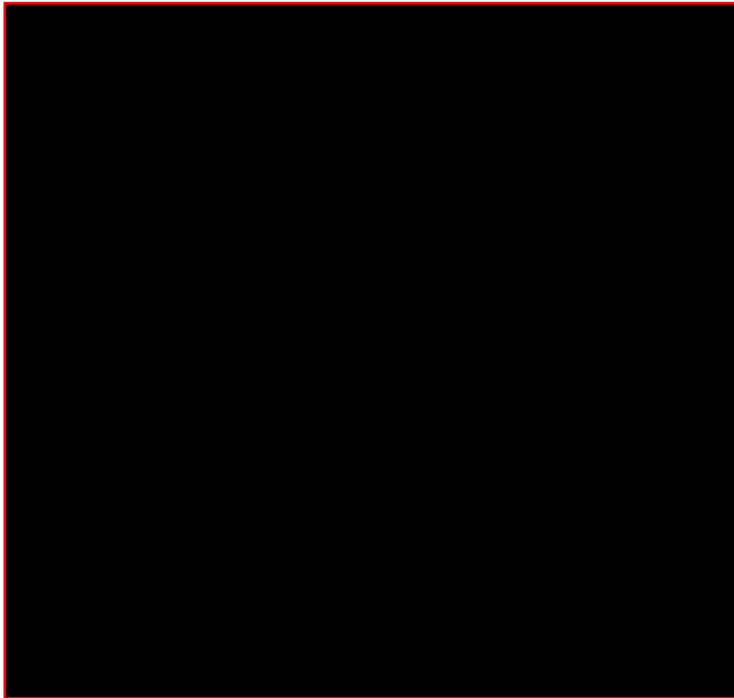




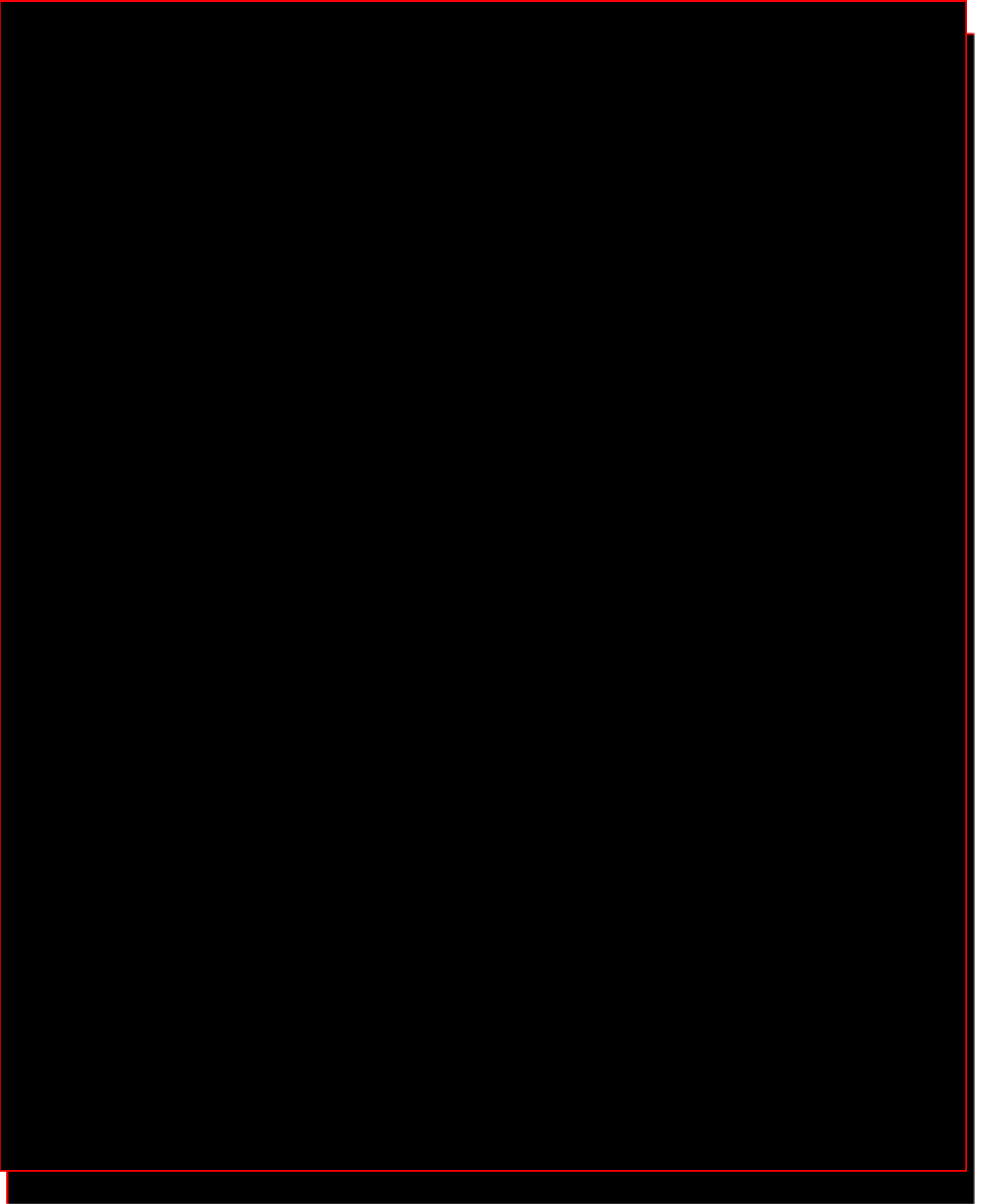


[REDACTED]

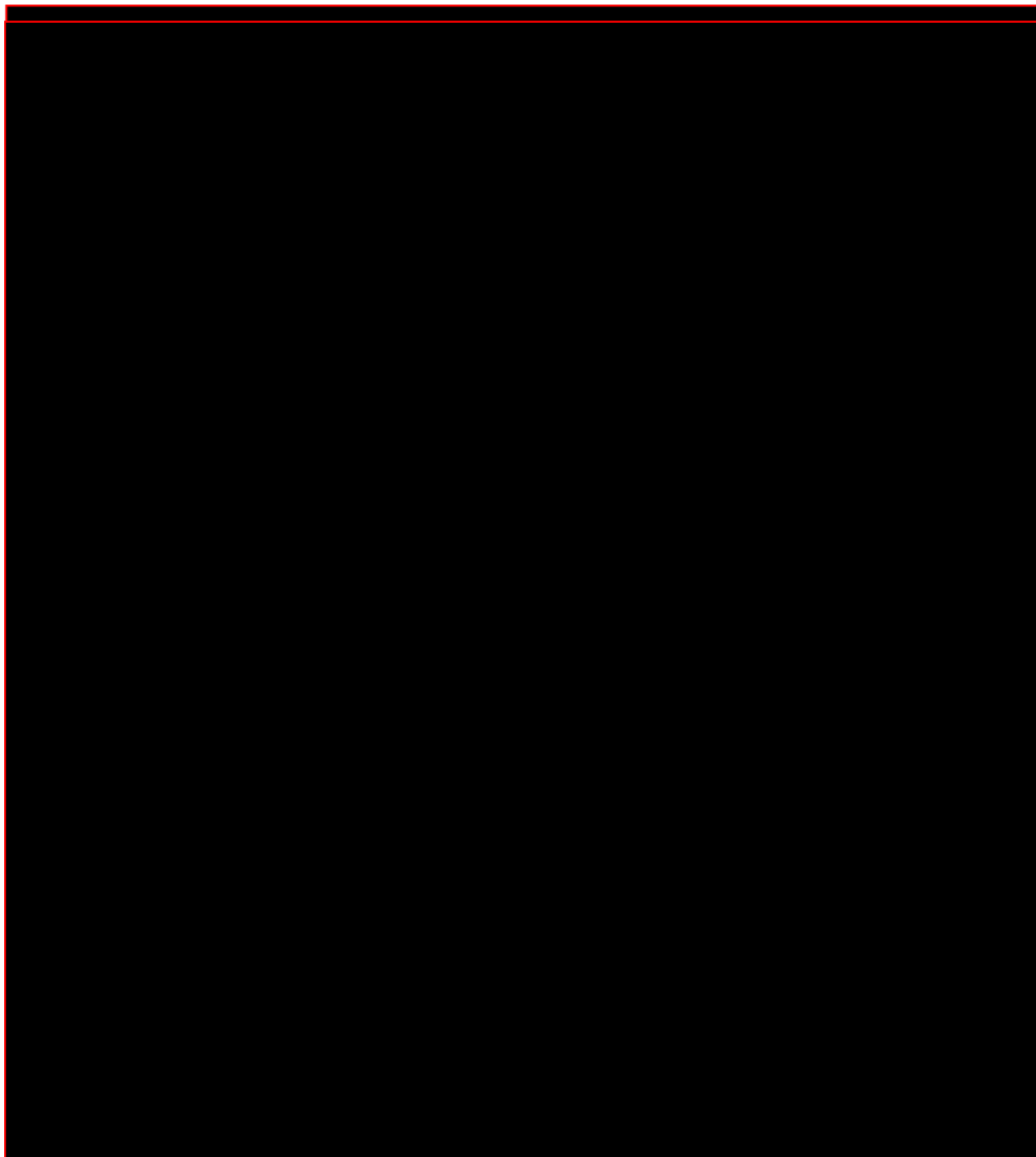
[REDACTED]



APPENDIX M: FACIT-F QUESTIONNAIRE

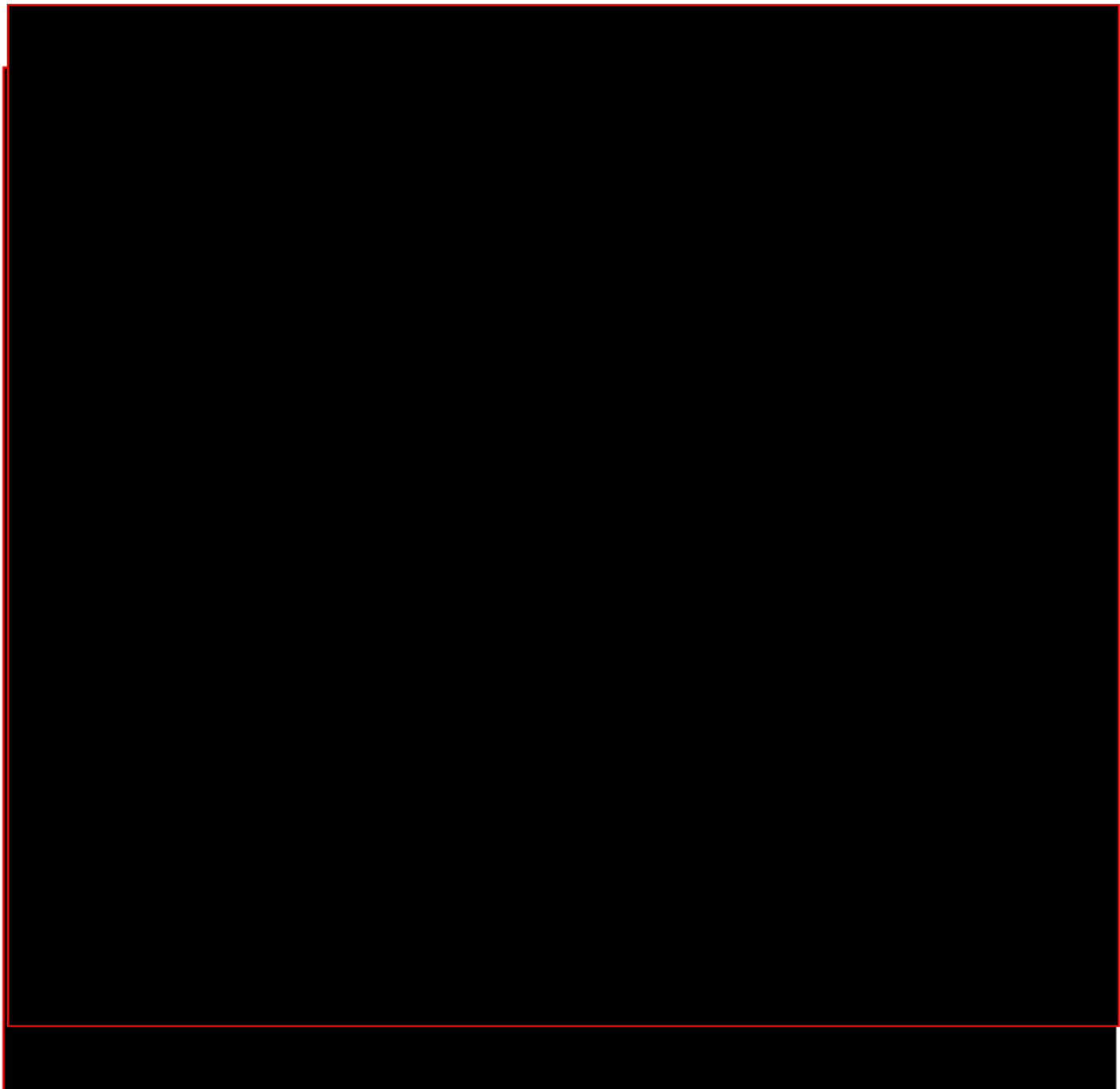






[illegible]

[REDACTED]



Service	Percentage of respondents
General practitioner	100%
Pharmacist	95%
Physiotherapist	85%
Psychologist	75%
Counsellor	65%

[illegible]

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[illegible]

[REDACTED]

████████████████████

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[REDACTED]

APPENDIX Q. PATIENT IMPROVEMENT QUESTIONNAIRE FOR SUBJECTS

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]